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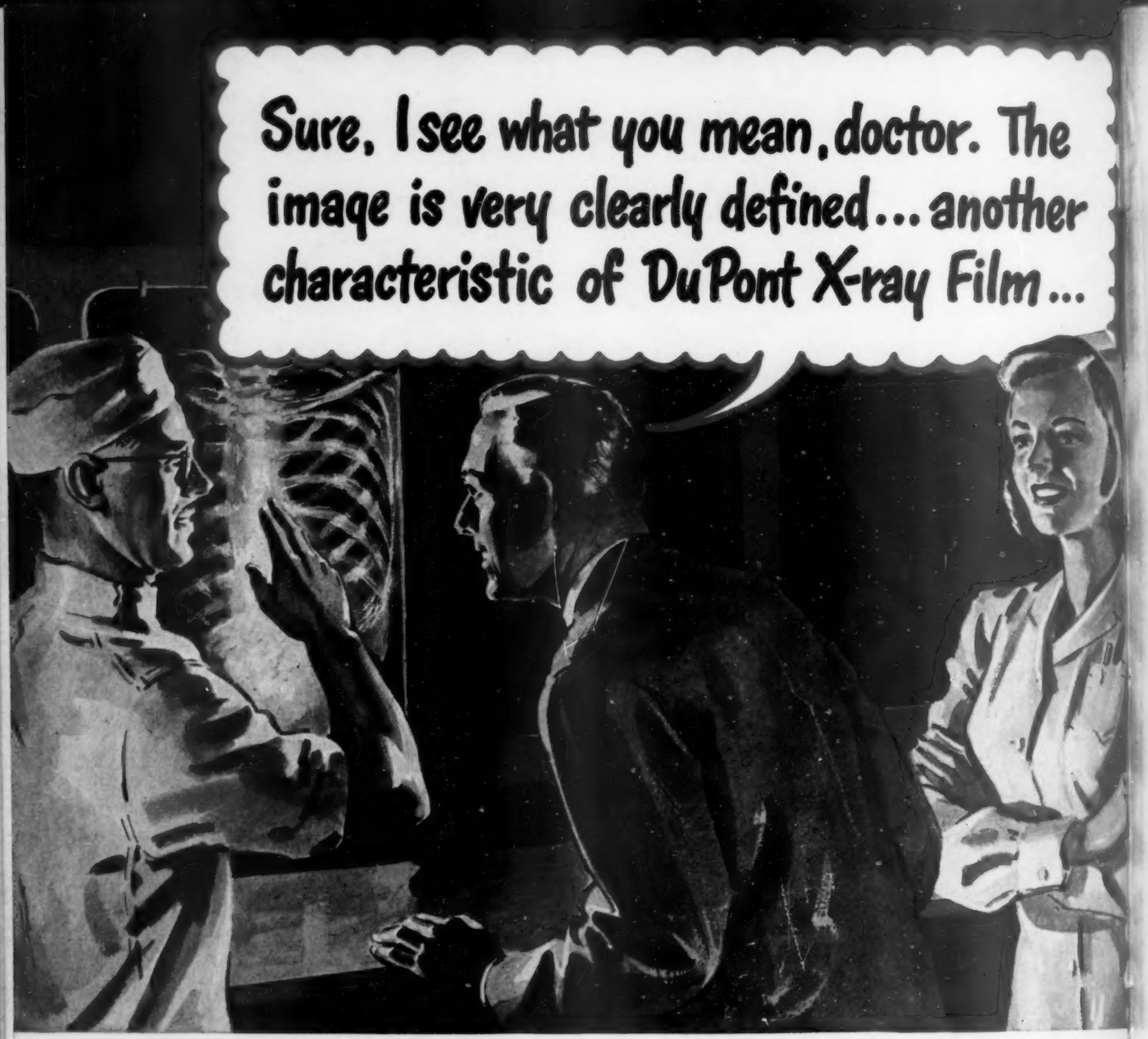

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. 60 AUGUST, 1948 No. 2

TECHNIQUES FOR APPLICATION OF THE BETATRON TO MEDICAL THERAPY*

By G. D. ADAMS, G. M. ALMY, S. M. DANCOFF, A. O. HANSON, D. W. KERST, H. W. KOCH, E. F. LANZL, L. H. LANZL, J. S. LAUGHLIN, H. QUASTLER, D. E. RIESEN, C. S. ROBINSON, *and* L. S. SKAGGS

URBANA, ILLINOIS

THE high energy roentgen-ray beam of the betatron has qualities which should make it useful in the treatment of deep-seated cancers. The rays are very penetrating, and have negligible lateral ecatter; therefore, it must be possible to irradiate any region anywhere in the body with great selectivity. The elementary biological effects of high energy rays, as far as examined, have been found to compare closely with those of rays of conventional energy. Thus the introduction of the betatron into cancer therapy is largely a question of developing appropriate techniques. Some of these techniques will differ from those used with conventional equipment because of the inherent characteristics of high energy radiation.

With the 22 million volt betatron the roentgen-ray beam emerges from a focal spot less than 0.2 mm. in diameter, requires about 1.6 cm. of lead to reduce it to half intensity, and falls off rapidly in intensity with angle, reaching half-intensity at 4 or 5 degrees from the central ray (Fig. 2). Many high energy primary electrons are scattered into the room from the target, but not in the direction of the roentgen-ray beam. Penetrating secondary electrons and roentgen rays are generated as the beam passes through matter such as the tube wall and these proceed mainly in the forward direction.

Measurement and evaluation of dosage present new problems. The dosimetry of high energy roentgen rays in absolute roentgens (r), with a standard open chamber, is impractical. Tissue doses can be measured in the usual way. The readings obtained with a 25 r condenser chamber of a Victoreen dosimeter, when embedded in a suitable phantom, are used as a preliminary standard. These readings have been, in turn, calibrated with regard to conventional roentgen rays (200 kv.) by means of quantitative biological tests. At present, we multiply high energy doses by a factor of 0.75 to obtain approximate biological equivalence with rays of conventional energy.

Depth doses, in conventional radiation therapy, are expressed in percentage of the

* From the Department of Physics, University of Illinois, Urbana, Illinois. This investigation was supported in part by a research grant from the National Cancer Institute of the National Institute of Health, United States Public Health Service.

surface dose. In a beam of high energy roentgen rays, the surface is not the locus of maximum energy absorption. The surface dose is, moreover, difficult to reproduce, because of the pronounced effect of stray electrons, and it is not a very significant quantity. It is recommended, therefore, that all tissue doses be expressed in percentage of the maximum tissue dose which, in a 22 million electron volt roentgen-ray beam, is about 4 cm. below the surface. Depth dose distributions have been obtained with thimble chambers in water and presdwood phantoms. In the latter phantom, photographic films were also used. The density above fog recorded on Eastman Industrial Film Type A is directly proportional to the dose over the range of practical density measurements. Further, the constant of proportionality seems independent of position with respect to surface of the phantom and center of the beam. For our purposes, then, photographic isodensity lines have been used as isodose lines (Fig. 4, *A* and *B*).

In addition to work on dosimetry, other recent experiments on the University of Illinois 22 mev. betatron have led us to some techniques for clinical application of the betatron, which are briefly described in the following paragraphs.

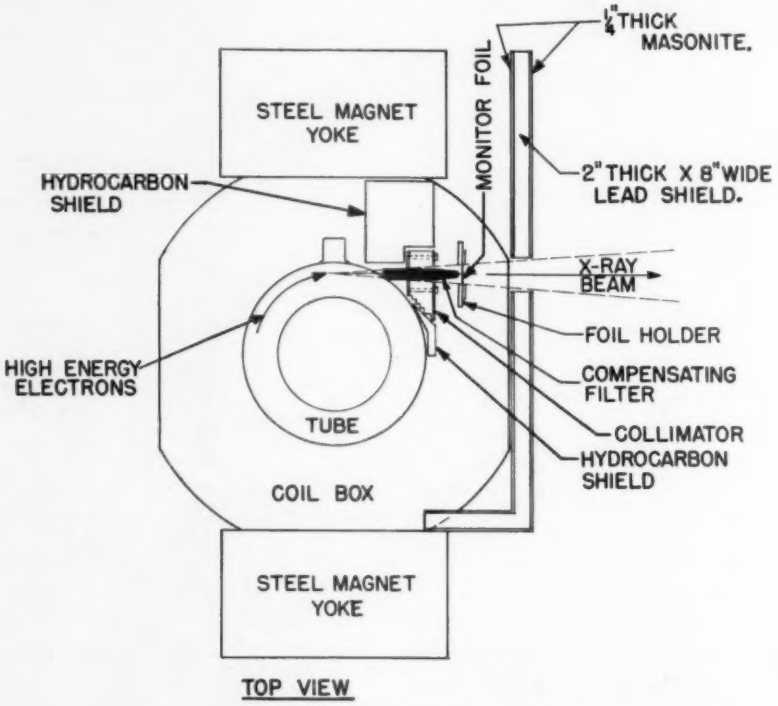

Fig. 1. Schematic top view of the 22 million volt betatron, showing arrangement of auxiliary instruments: collimator, electron and roentgen-ray shields, compensating filter, monitor foil.

Collimation of Beam. The function of the collimator is to control the size and shape of the very penetrating beam by absorbing sharply and sufficiently radiation outside of the desired cross-section. A collimator consists of lead 2½ inches thick with a channel of desired shape. It is placed between the coil boxes of the betatron, as near the accelerating tube as possible, in order that its weight and bulk be small and that secondary electrons produced in the collimator will be deflected by the magnetic field of the betatron. The collimator is built of 1/32 inch sheets of lead alternating with insulating sheets of paper. This construction

suppresses eddy currents to a value which does not interfere with the circulating beam of electrons in the nearby accelerating tube.

The lead of the collimator transmits 6 per cent of incident roentgen-ray intensity at 20 mev., and this is further reduced to less than 1 per cent by a second solid lead shield. The disposition of collimator and outer lead shield is shown in Figure 1 and its effect in defining the beam in Figure 2. about 0.5 per cent of the beam intensity, and that at some positions in the room within 10 feet of the beam the level was less than 0.01 per cent of the beam intensity. Operating personnel, outside the room, receives less than 0.01 r even on very prolonged runs, with a beam intensity of about 50 r per minute at 1 meter.

Neutrons are produced in material near the tube target, but measurements have

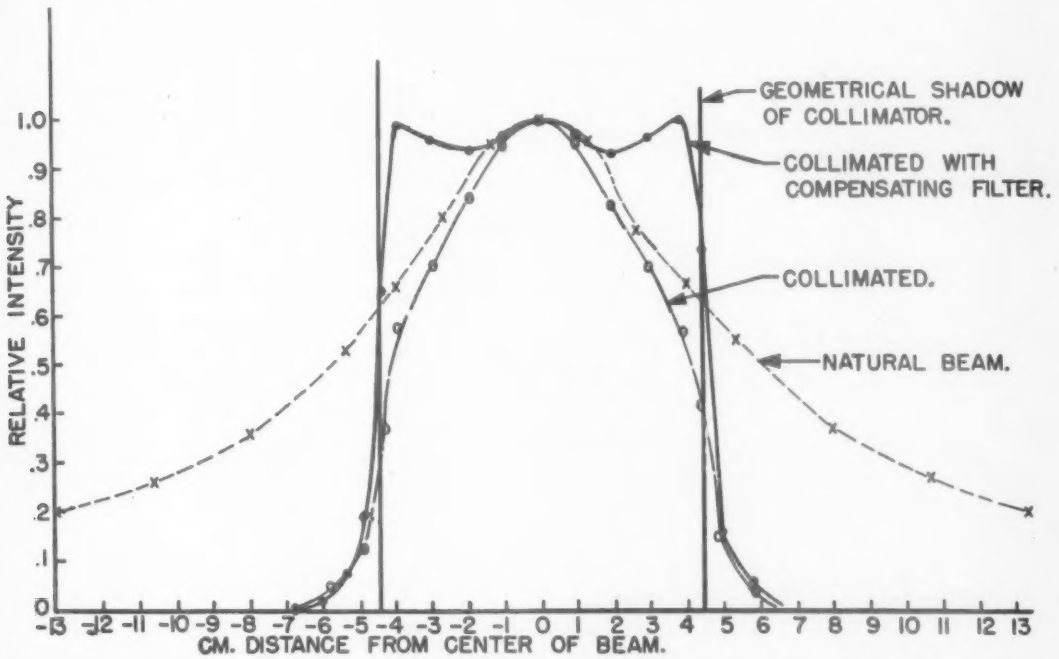

Fig. 2. Distribution of intensity across the beam. (Note: the cross section through the natural beam has been taken under conditions slightly different from those for the two collimated beams.)

Shielding of Stray Radiation. Two kinds of shields were used: (1) material of low atomic number to absorb stray electrons with relatively low production of secondary roentgen rays, and (2) material of high atomic number, such as lead, to absorb stray roentgen rays. Hydrocarbon shields placed as shown in Figure 1 absorb the electrons which are moving in curved paths but generally forward and the outer lead shield takes out the stray roentgen rays. Total ionization intensity is thereby reduced to safe levels. Typical measurements showed that at a distance of 1 foot from the primary beam, the total stray intensity was shown that outside the shields and under typical operating conditions, fast and slow neutron backgrounds were everywhere at a very safe level.

Compensating Filter. Filters are used to improve the characteristics of the beam in two ways: (1) by selective absorption to reduce the low energy content, and (2) by proper shaping to make the intensity distribution across the beam fit a predetermined scheme. The change in quality by selective absorption accentuates the transition rise from surface to maximum dose and increases depth doses. Both effects are small but appreciable. On the other hand,

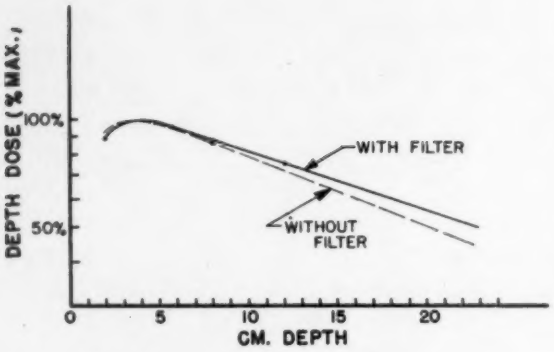

Fig. 3. Depth dose—center line. Water phantom at 100 cm. Circular beam, 11 cm. diameter. Thimble chamber measurement.

shaping the isodose surfaces is of considerable importance.

The basis for choice of filter material differs from that for conventional roentgen rays. In a continuous spectrum ranging from 0 to 20 mev., light material such as carbon transmits best at energies near the 20 mev. Hence a filter of carbon shifts the spectral distribution toward higher energy and the beam is more penetrating in tissue-like material. A heavy material such as lead has the opposite effect since it transmits best at about 3 mev. This is because of pair production which increases with energy and markedly with atomic number. A copper filter, intermediate in atomic number, leaves the quality and penetration practically unaltered, except for strong absorption below 2 or 3 mev. and would be as

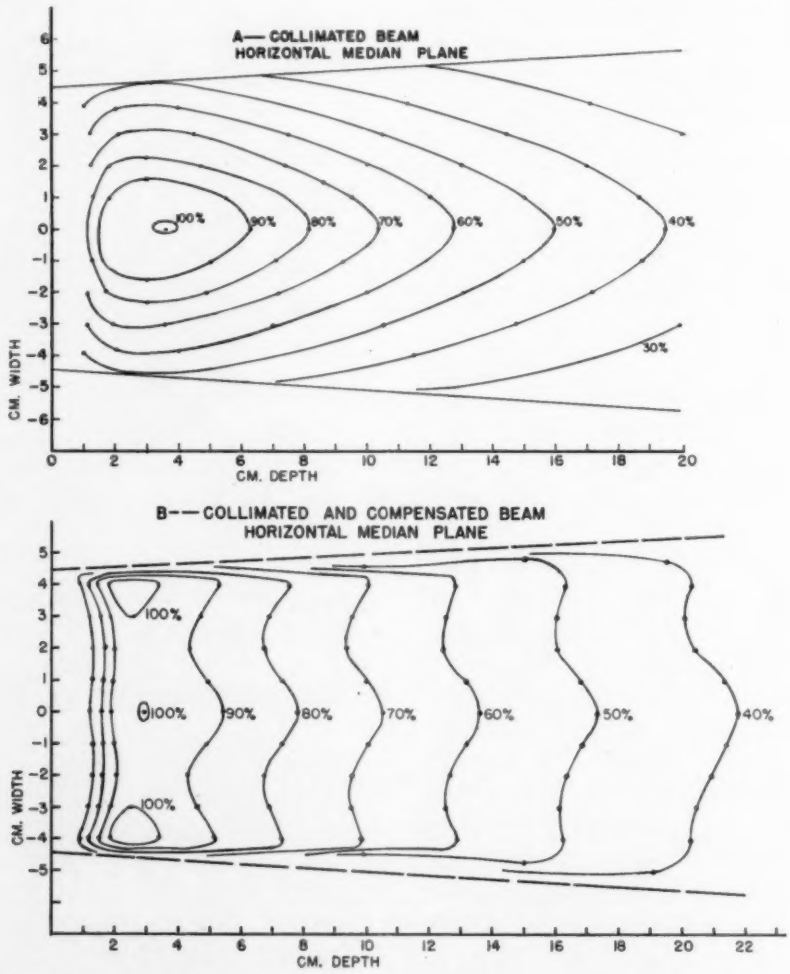

Fig. 4. Depth dose distributions. Presdwood phantom at 75 cm. Circular beam of 9 cm. diameter. Photographic measurements with thimble chamber spot checks.

suitable as carbon for shaping isodose surfaces.

Our compensating filter is a cigar-shaped block of graphite tapered so as to present less material as the beam intensity falls off from its center. It was intended to produce flat isodose levels approximately normal to the direction of the beam. It is placed in the collimator aperture and hence in the betatron magnetic field which deflects secondary electrons generated in the filter (Fig. 1).

The effects of the compensating filter on depth dose distribution are shown in Figure 3. The shape of the beam with and without filter appear in Figure 2, and the corresponding isodose levels in a presdwood phantom in Figures 4, *A* and *B*.

Monitoring of Irradiations. Monitoring of a dose administered in a given treatment involves some difficulties when the irradiated object encompasses the whole collimated beam. In such a circumstance, the most reliable solution is a transmission monitor placed between target and object. One technique of transmission monitoring uses the radioactivity induced in a thin foil. The foil is not sensitive to primary electrons, and the secondary electrons it produces are swept out by the magnetic field in which it is situated (Fig. 1). The forty minute (gamma, n) activity induced in a 0.002 inch zinc foil by irradiations of a few minutes' duration is enough to allow dosage determinations with a statistical error of less than 1 per cent. The activity of the foil is calibrated by comparison with the standard ionization chamber. However, the calibration holds only at the energy at which it was taken. During irradiation of an object the roentgen-ray output of the betatron is approximately indicated by an ionization chamber placed in the stray radiation field.

A detailed description of the techniques and devices described above will be published later in this JOURNAL.

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SOME DEPTH DOSE STUDIES OF ROENTGEN RAYS FOR ENERGY LEVELS FROM 20 TO 100 MILLION ELECTRON VOLTS

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I. INTRODUCTION

THE development of higher energy electron accelerators[2,3,14] has made it possible to investigate the depth dose of roentgen rays for energy levels much higher than the conventional voltages now generally used in therapeutics. Experimental depth dose measurements with roentgen rays up to 4 million electron volts have been reported by Trump, Moster and Cloud[12] and for energies from 5 to 20 mev by Koch, Kerst and Morrison.[4] The well known objective of radiation therapy is, of course, the destruction of malignant tissue with the minimum of injury to surrounding tissue within the volume of the body medium that the radiation must pass through. It is the purpose of this paper to present some absorption studies obtained with roentgen rays in the energy range from 20 to 100 mev, which shows the distribution of energy absorbed in a phantom at these higher energy levels, but with no evidence which would indicate or evaluate their therapeutic effectiveness as compared to lower energy roentgen rays generally used today in therapeutic treatment. The possible biological effectiveness of these very much higher roentgen-ray energies can only be adequately evaluated after careful and extensive investigations by the radiologists and the biologists working with these radiations.

II. 100 MEV ELECTRON ACCELERATOR (BETATRON)

This study was made using roentgen radiation generated by the 100 mev electron accelerator in our Laboratory.[14] The toroidal vacuum tube in this machine is made of molded Pyrex glass, and the roentgen-ray target was a tungsten rod 150 mils in diameter. The inherent filtration of the tube through which the beam emerges was $\frac{5}{8}$ inch of borosilicate glass. Since the roentgen rays coming from the tungsten target are essentially thin target radiation there was no appreciable metal filtration within the toroid for the emerging roentgen-ray beam. Roentgen rays can be generated from this machine at all energy levels up to 100 mev and most of the absorption measurements to be reported here were made in 10 mev steps in roentgen-ray voltages.

III. FILM-DENSITY METHOD OF DEPTH DOSE MEASUREMENTS

The distribution of the high voltage roentgen-ray energies absorbed in a pressboard phantom has been investigated by a film technique. From measurements of the densities obtained on different parts of a film placed within the phantom, it is possible to deduce the roentgen-ray energy absorbed by ionization in various parts of the phantom. The film used in this work was Eastman type M. The roentgen-ray voltages employed in this work were above those for which type M film characteristic data have been published. Film characteristic curves were made with 100 mev roentgen rays to compare with the published data given by the Eastman Kodak Company[11] for 200 kv. roentgen rays.

The simple relation between density and exposure may be used as a relation between density of the film and the amount of roentgen-ray energy absorbed in any area of the film. The term "density" is here

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used in the manner conventional to photographic work; that is, the density of the silver deposit produced on a film is numerically equal to the logarithm of the opacity of the film, where opacity is the ratio of light incident upon the film to light transmitted through the film. The density of the shadows on the emulsion was measured by an Ansco-Sweet densitometer which gives direct readings.

The normal range of this densitometer is from 0.00 to 3.00 in marked density steps of 0.02. One may easily read half-divisions, giving variations of 0.01. Adjustment is achieved, first by varying the brightness of the light source with a rheostat to cause the instrument to read 0.00 with no film in the aperture, second by placing a film of standard density of 3.00 in the aperture, and adjusting the instrument to read 3.00. The calibration of the instrument is further checked with standards of intermediate density. The range of the instrument for some measurements was extended to a density of 3.60 by using a stronger light source and a larger aperture.

The densitometer was found to repeat density measurements of given films with an error of less than 1 per cent. The area of the film measured is 0.079 cm.^{2} The ability to measure such a small area, to measure continuously over all parts of the film, and to measure film exposed very close to the phantom surface are advantages of the photographic method of phantom operation.

The relative ionization was measured with the standard Victoreen r thimble and meter. The least error in reading the 25 r scale is about $\pm$0.1 r for which the scale is marked every 0.5 r. Many measurements in making the film characteristic curve were between 5 and 10 r, so the relative error introduced is probably about 2 per cent. It should be noted that in comparing films or points on a film, this error does not enter the measurement.

To determine the necessary relation between ionization and density the following procedure was used: If the film and thimble are exposed to the same part of the roentgen-ray beam simultaneously the presence of one will affect the response of the other, due to scattered and secondary radiation. Simultaneous exposure is not necessary, for a relation between two variables may be established in terms of the dependence of each of these variables upon some third variable. This was accomplished by alternately exposing film and standard thimble under identical conditions while an ionization chamber monitor was kept in a fixed position to one side. Thus a relationship between film density and relative ionization is established. The film was exposed in a cassette made of two pieces of lead, each $\frac{1}{4}$ inch thick. The r thimbles were also jacketed in lead $\frac{1}{4}$ inch thick. This thickness was chosen because at 100 mev it gives nearly maximum intensification. To obviate any question of the non-dependence of the film characteristic curve upon the absorbing material, this step was later done in a pressboard phantom by exposing five films for different periods of time and subsequently developing them simultaneously. The film and thimble were alternated in pressboard at a depth of 9 cm in the phantom while the monitor was kept in a fixed position. The films were developed at 68° F. for eight minutes. Then the films were rinsed in a shortstop for one minute, and then fixed. The developing time of eight minutes was chosen as standard procedure in this study for two reasons. First, eight minutes' development gives high contrast without unduly high fog level, and second, the slope of the time-gamma curve is not as steep at eight minutes as it is for shorter times, so the relative errors in density introduced by inequalities in development would be minimized. Development longer than eight minutes gave higher fog level and densities above the usable range of the densitometer.

The film characteristic curves for 100 mev radiation and for 200 kv. radiation with Eastman Kodak type M roentgen film are shown in Figure 1. The values obtained in lead and in pressboard for 100 mev radi-

ation fell on the same curve A, within the experimental error. On the same plot the Eastman Kodak Co. data shown on curve B for 200 kv. radiation falls practically on the same line. This justifies the assumption that the relation indicated in curve A between film density and relative ionization holds for all energy levels between 20 and 100 mev.

A correction for variations in fog level density due to age, etc., must be made. The value of fog level experienced when making the film characteristic curve was 0.24. This was arbitrarily assigned to be the normal value, and corrections were made for variations from this value.

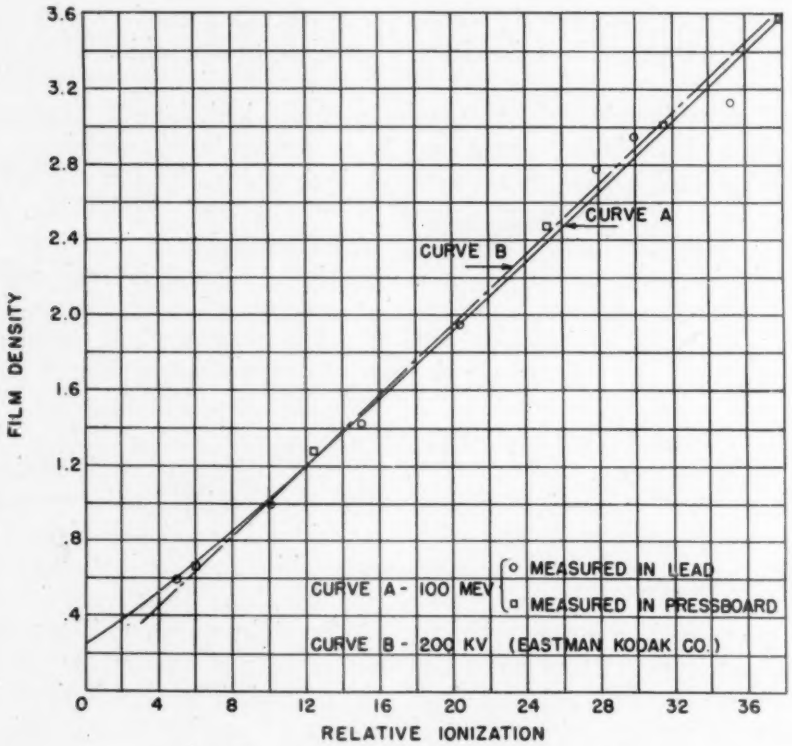


FIG. 1. Film characteristic curve.

The Phantom. The phantom used in this study (Fig. 2) consists of a "U"-shaped wooden clamp which holds 56 sheets of pressboard (Masonite tempered board), the dimensions of each being 14 by 17 by $\frac{1}{4}$ inch. The scale shown in the photograph is in inches. The clamp is built of hard wood with no metal parts, the joints and fastenings being made with glue and wooden dowels. The pressboard was found to have a density of 1.083 ± 0.005 gm/cm^3. The mass of various pieces of the same area differed, but micrometer measurements showed a corresponding variation in thickness. Film cassettes were made by placing the film between two sheets of pressboard and binding all the way around with opaque scotch tape. A film cassette made of two sheets of pressboard bound with white tape is shown in the center of the phantom. The phantom may be arranged in any desired position relative to the betatron. The minimum working distance between roentgen-ray target and front plane of phantom, limited largely by the dimensions of the 100 mev betatron itself, is 125 cm.

Films were exposed in the phantom in two distinct positions. In one, the film was placed so that its long dimension lay along the axis of the roentgen-ray beam, giving an "axial" exposure. Thus one end of the film was at zero depth in the phantom and the other end at 43.2 cm. depth. In this

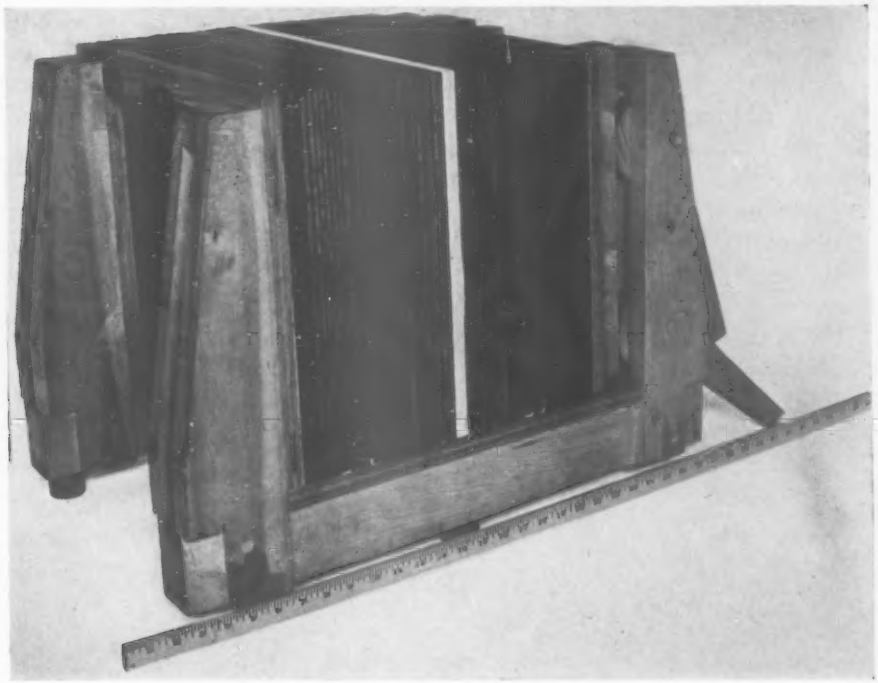


Fig. 2. The pressboard phantom.

Fig. 3. Photograph of 50 mev roentgen-ray beam in phantom.

case the phantom was placed so as to be symmetrical with the axis of the beam. A film so exposed shows density as a function of depth and at right angles from the axis at the same time. The second method is to expose the film so that the axis of the beam is perpendicular or "orthogonal" to the center of the film, as in taking a common roentgenogram. These orthogonal films show the cross-section distribution of the beam for different depths and distance from the target. It was useful to expose several orthogonal films simultaneously, one behind the other at different depths. The orthogonal films provided the best methods of evaluating the "skin dose". For the film placed on the source side of the phantom a cassette is made of a piece of opaque celluloid 0.16 mm. thick and a piece of pressboard bound at the edges. Thus a film may be placed in the phantom from a depth of 0.16 mm. in organic material up to 35 cm. in steps of 0.63 cm. In all cases, the films were developed by the procedure previously described. Films exposed simultaneously were developed simultaneously.

Since the ionization produced in a given volume of air is a small fraction of that produced in an equal volume of pressboard, care must be exercised to reduce the air voids between the pressboard sheets in the phantom to a minimum. This is accomplished by applying the clamping mechanism uniformly.

Fig. 4. Photograph of 100 mev roentgen-ray beam in phantom.

Figures 3 and 4 show photographs of the roentgen-ray beam taken on axial films in the phantom at roentgen-ray voltages of 50 and 100 mev. These are 14 by 17 inch films. These films were made in the phantom at 132 cm. target distance. No collimation or filtration of the betatron beam was used in taking these photographs. The beam with the 100 mev radiation is inherently more collimated and more penetrat-

ing than the 50 mev radiation.

Isodose Charts. The isodose curves shown here (isodose charts for 50, 70, and 100 mev) (Fig. 5, 6, 7) have been made by densitometering the axial phantom films. For comparison on a percentage basis the film density readings have been converted to relative ionization by using the data obtained in Figure 1. Then the peak value is considered 100 per cent, and lower ionizations are expressed in percentages of the peak value.

Densitometer readings of several axial films made at the same roentgen-ray voltage give good agreement in the values shown in these isodose charts. Axial films have been exposed with the plane of the film both horizontal and vertical. Analysis of these has shown the distribution of density along and across the axis to be in good agreement. A three dimensional concept of the absorption pattern may be had by rotating an axial isodose chart about the axis.

The isodose charts illustrate the same trends that have already been pointed out in discussion of the photographs; namely, at higher roentgen-ray voltage the peak of ionization occurs at a greater depth, and the angular width enclosing 50 per cent of the roentgen-ray beam is less.

Figure 8 shows the relative ionization along the axis of the roentgen-ray beam as a function of depth at different energy levels. These data for each energy level were plotted from orthogonal exposures for which twelve films were placed at different depths in the phantom and the whole family of films were exposed and processed simultaneously. The point of maximum density on each of the twelve films was located and measured with the densitom-

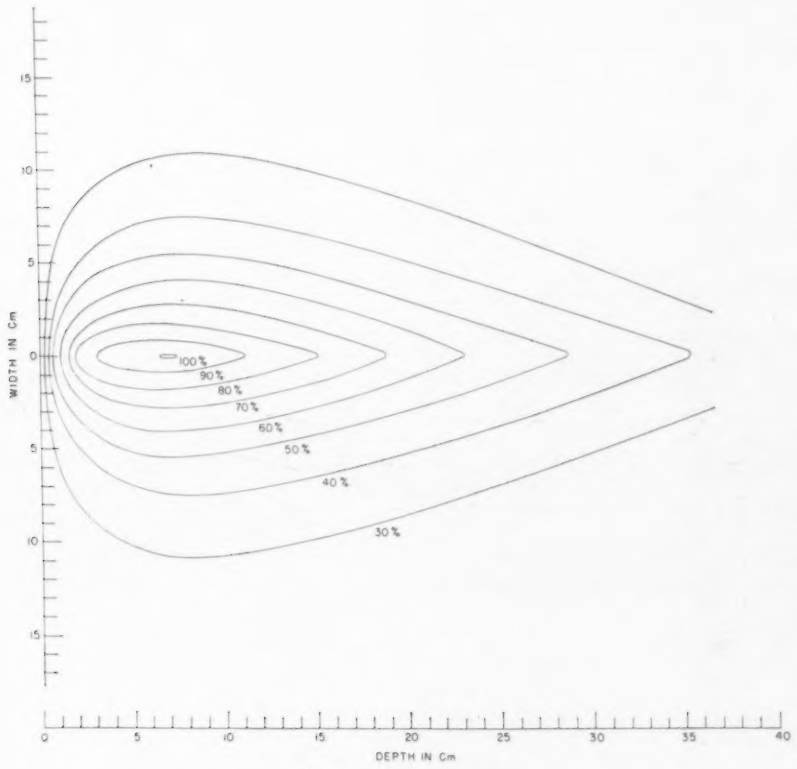


Fig. 5. 50 mev isodose chart. This map was made from an axial film exposed at 132 cm. target-phantom distance with no limiting aperture.

eter and the corresponding relative ionization factor obtained from Figure 1. Unexposed films were developed with each group and measured to obtain the correction factors for any variation in fog level. All of the values of relative ionization for each energy level were multiplied by the reciprocal of the relative ionization value of the first film taken at 0.016 cm. depth, in order to bring the relative ionization for the approximate entrance point in every case to unity. This permits one to compare relative ionization in depth for different roentgen-ray voltages in terms of unit absorption at an entrance depth of 0.016 cm. It is readily seen that with increasing voltages the peak value of ionization not only occurs at a greater depth but when the entrance dose is held constant these peak values are greater.

It is interesting to note that a semi-logarithmic plot made from data obtained from Figure 8 gives a linear relation within experimental error between the relative peak ionization and the depth of the peak for the different roentgen-ray voltages.

The depth dose measurements presented in Figure 8 are in reasonable agreement with similar measurements in a pressboard phantom with the 100 mev betatron made by Failla, Braestrup, Klaiber and Charlton (Fig. 9) in which they used an ionization chamber method in place of the film-densitometer technique. The ionization chamber method used has been described by Failla.[1] The target-phantom distance in this case was 116 cm. The dotted curves in Figure 9 for energies up to 20 mev are from data reported by Koch, Kerst and Morrison.[4]

The peak absorption for 50 mev comes at a slightly lower depth for the ionization

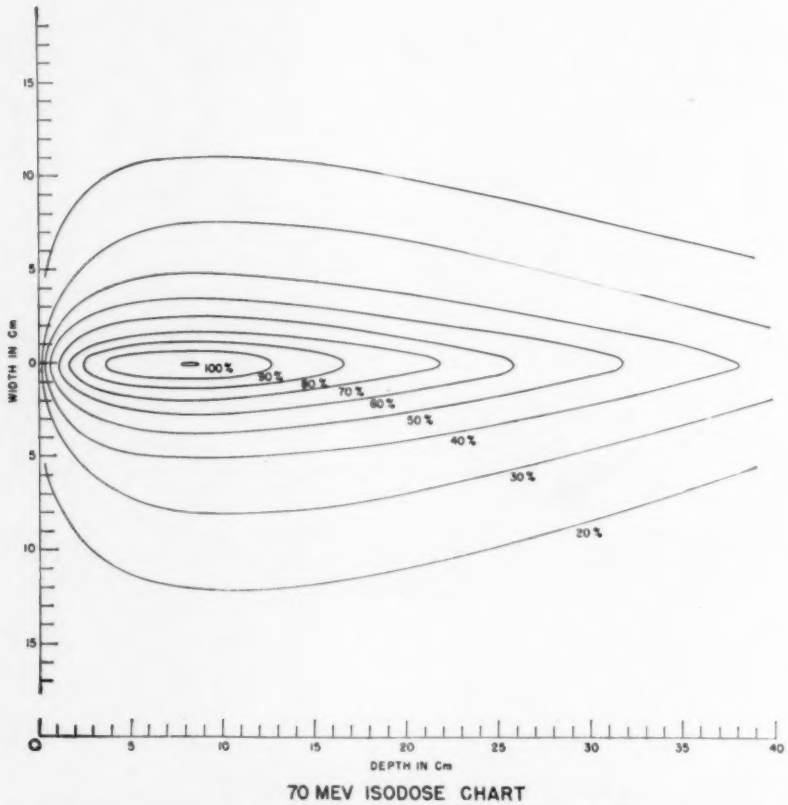


Fig. 6. 70 mev isodose chart. This map was made from an axial film exposed at 132 cm. target-phantom distance with no limiting aperture.

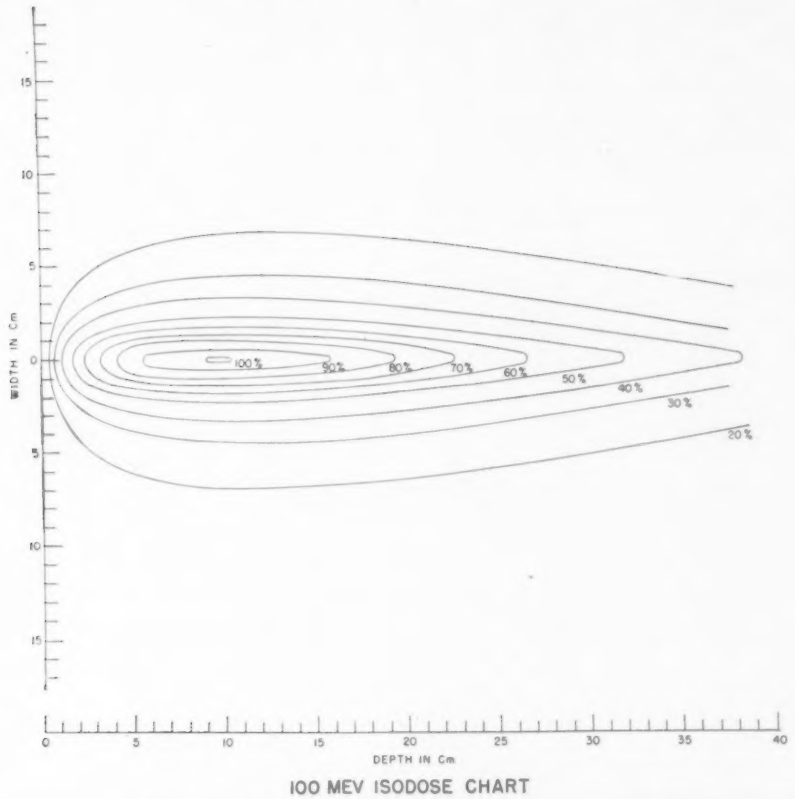


FIG. 7. 100 mev isodose chart. This map was made from an axial film exposed at 132 cm. target-phantom distance with no limiting aperture.

method than that obtained for the film densitometer technique. This was apparently due to the fact that in the ionization chamber measurements, the pressboard phantom was closer to the target; this effect will be discussed below. No collimation nor filtration of the beam was used in these experiments to filter out the electrons. The differences in peak ionization values between Figures 8 and 9 at different roentgen-ray voltages are dependent upon the arbitrary depth in the phantom chosen as the reference point for unit absorption.

In Figure 10, plotted to give the same peak ionization for different roentgen-ray voltages, it is apparent that while the entrance dose is decreasing with rising energy levels, the exit dose is increasing. One can readily see that a given percentage of peak energy is absorbed at different depths for different voltage levels. These data were obtained with a target-phantom distance of

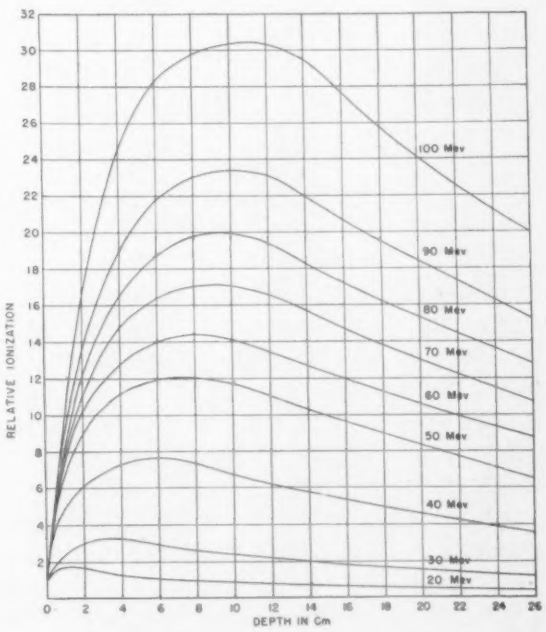


FIG. 8. The relative ionization at any depth in the phantom caused by a unit entrance dose, at energy levels from 20 to 100 mev.

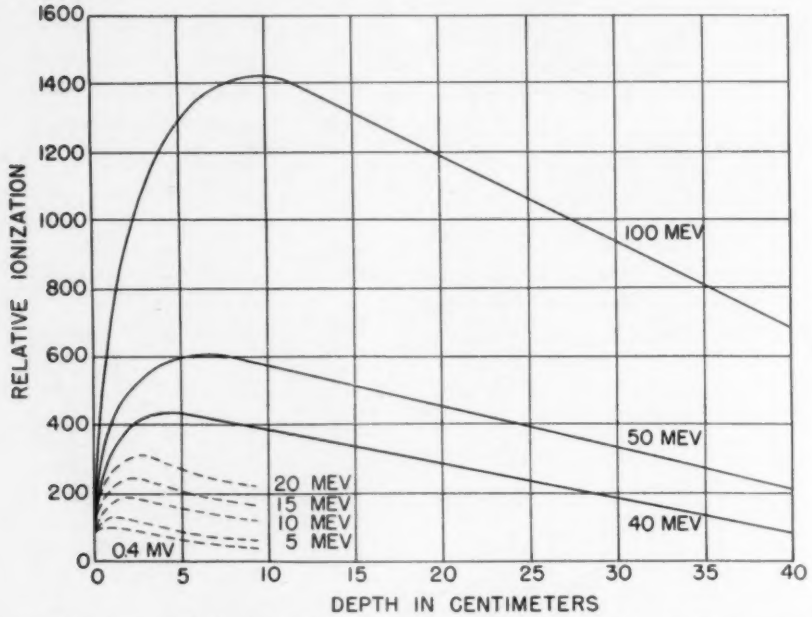


FIG. 9. Ionization chamber method of depth dose measurement in pressboard phantom using high energy roentgen rays from betatron.

132 cm. If this distance is decreased, more attentuation due to inverse square effect will be experienced, the depth of the peak will decrease and the exit dose will decrease. The converse will occur at greater target-phantom distance. Were it not for variations in intensity across the field of the roentgen-ray beam in the relatively small angles enclosing 50 per cent of the total intensity, it would be desirable to use the

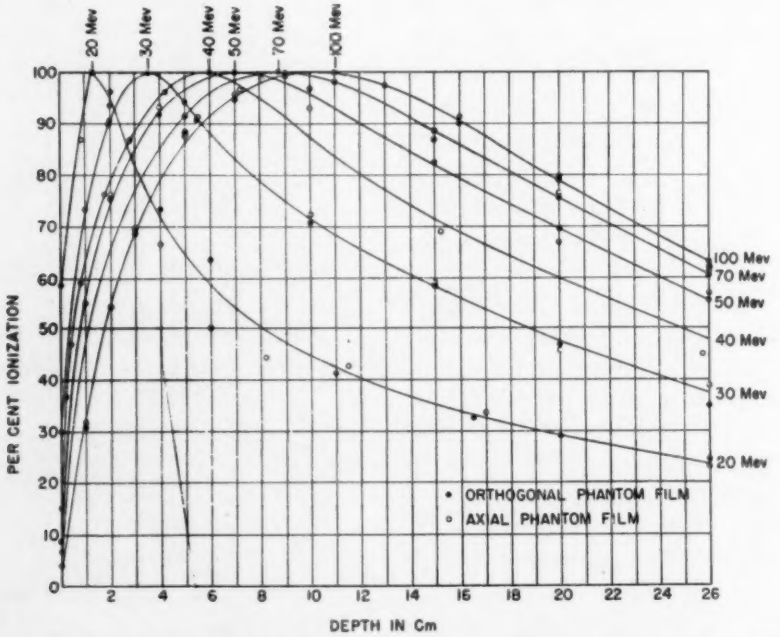


FIG. 10. The per cent of peak ionization occurring at any depth in the phantom for the various roentgen-ray voltages.

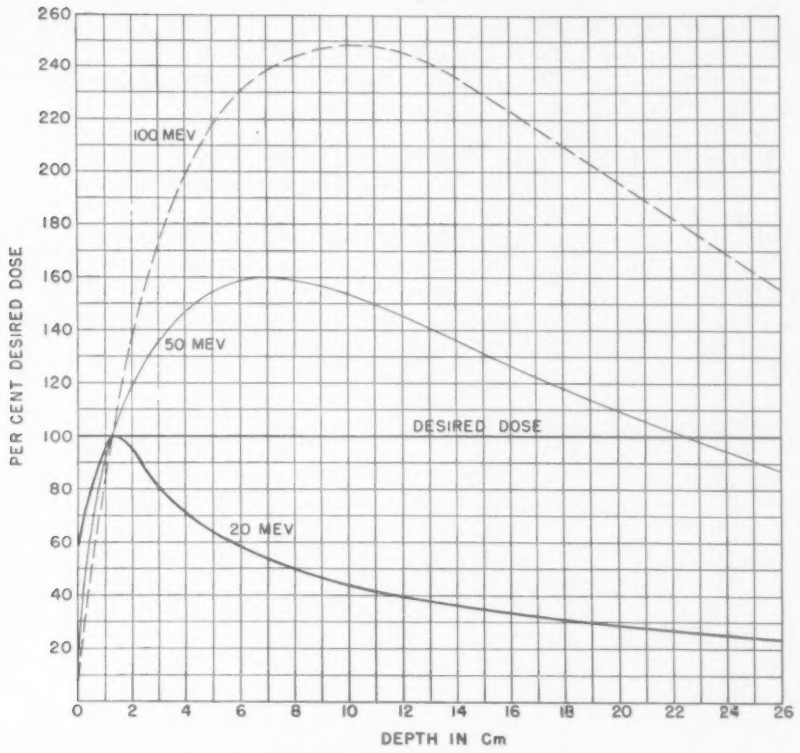


FIG. 11. Energy distribution in the phantom when producing unit ionization intensity at 1.5 cm. depth with 20, 50 and 100 mev roentgen rays.

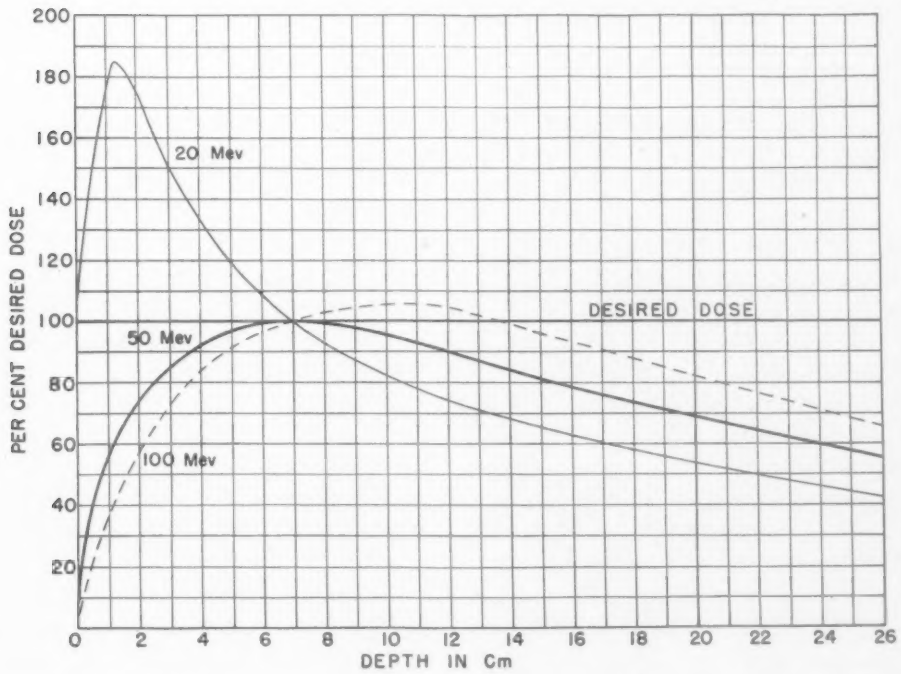


FIG. 12. Energy distribution in the phantom when producing unit ionization intensity at 7 cm. depth with 20, 50, and 100 mev roentgen rays.

radiation at the shortest possible target-phantom distances. With due consideration given to both entrance and exit doses it is possible to choose the appropriate roentgen-ray voltage to cause the peak ionization to occur at any desired depth within the phantom.

Figures 11 and 12 have been replotted from data given in Figure 10 to bring out clearly the value of choosing different roentgen-ray energies when it is desired to get maximum energy absorbed at a specific depth and a minimum absorption elsewhere within the phantom. Using unfiltered radiation, 20 mev roentgen rays are obviously more favorable for 1.5 cm. depths and 50 mev roentgen rays for 7.0 cm. depth.

It should be stressed that the exit dose rather than the entrance dose becomes the limiting factor for energies beyond 30 mev. This will be apparent from Figure 10, from which it can be seen that for the same peak dose the higher the energy the greater the exit dose.

The value of the half intensity angle in the roentgen-ray beam is rapidly decreasing as the roentgen-ray energy level increases. At 20 mev the half-value cone is slightly over 9°; at 50 mev it is 4° and at 100 mev, it is 2°. While the half intensity angle is to some extent dependent on the inherent filtration interposed between the roentgen-ray target and the phantom, it is in the main an inherent property of the mechanism of roentgen-ray generation by electron impact on target bodies at these very high energy levels. Figure 13 shows the angular energy distribution for roentgen-ray voltages ranging from 20 to 100 mev, determined by densitometry of films orthogonally exposed in the phantom at the depth of the peaks for the respective voltages as shown in Figure 10. For any roentgen-ray voltage, the roentgen-ray intensities are very nearly uniform for all points around the circle at any given radius from the axis of the beam. Since the energy distribution is not uniform across the beam

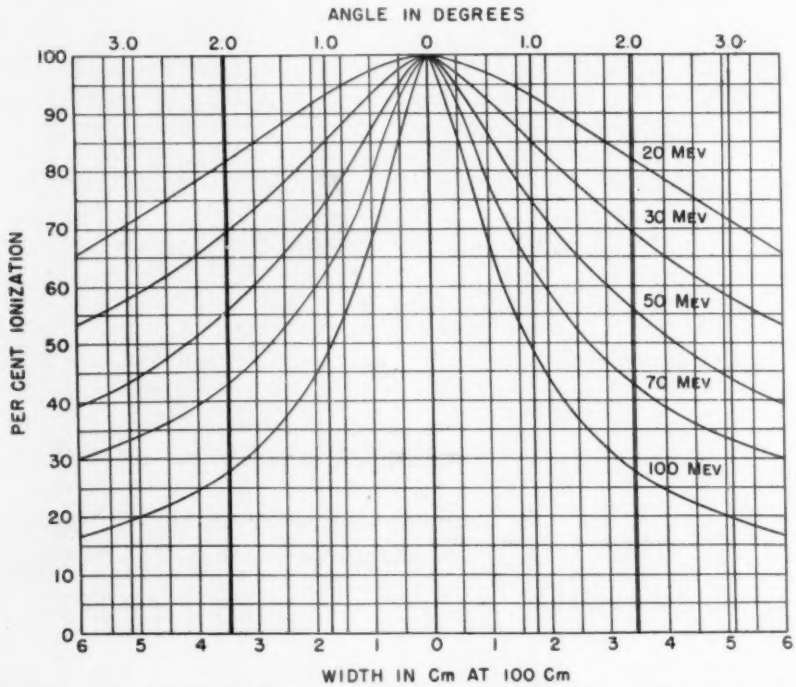


Fig. 13. The per cent ionization at different distances from the axis of the roentgen-ray beam for a target distance of 100 cm. Since the angular width of the beam at any per cent ionization level is independent of target distance, an angular scale is shown also.

it may be desirable to show the size of fields enclosing all intensities down to 80 per cent of the maximum intensity in the center of the beam for different energy levels. Table 1 shows the target-phantom distances that would be required to maintain the ionization intensity above 80 per cent of the maximum value for different roentgen-ray voltages and different sizes of fields.

The distribution of peak ionization in the pressboard phantom will shift to some extent with different target-phantom distances. Figure 14 for 50 mev roentgen rays indicates that with increasing distance the depth for peak ionization and the exit dose at 26 cm. increase slightly. These shifts may be attributed to the inverse square law and indicate the desirability of having the target-phantom distance as short as the distribution of ionization across the desired field will permit. If in Figure 15, we let E be the radiant flux incident per unit area of the primary roentgen-ray beam, then E at any distance in the phantom around the axis of the roentgen-ray beam will be subject to variations due to the distance X and also to absorption in the phantom. The variation due to distance alone is

$$\frac{\delta E}{E}=\left(-2\,\frac{dx}{x}\right)$$

from the inverse square law. The variation due to absorption alone is

$$\frac{\delta E}{E}=(-\mu dx)$$

where μ is the coefficient of absorption in cm^{-1}, and x is the distance from the target to any point in the phantom. If X_1 is the

TABLE I

TARGET-PHANTOM DISTANCE AND FIELD WIDTH ENCLOSING 80 PER CENT OF MAXIMUM IONIZATION FOR DIFFERENT X-RAY VOLTAGES

	X-Ray Field Diameters in cm.					
	1	2	5	10	15	20
Mev	Target-Phantom Distance in cm.					
100	78	156	390	780	1170	1560
50	32	64	160	320	480	640
30	22	44	110	220	330	440
20	14	28	70	140	210	280

Note: Field diameter at 100 cm. is 1.3 cm. for 100 mev; 3.1 cm. for 50 mev; 4.5 cm. for 30 mev; and 7.4 cm. for 20 mev.

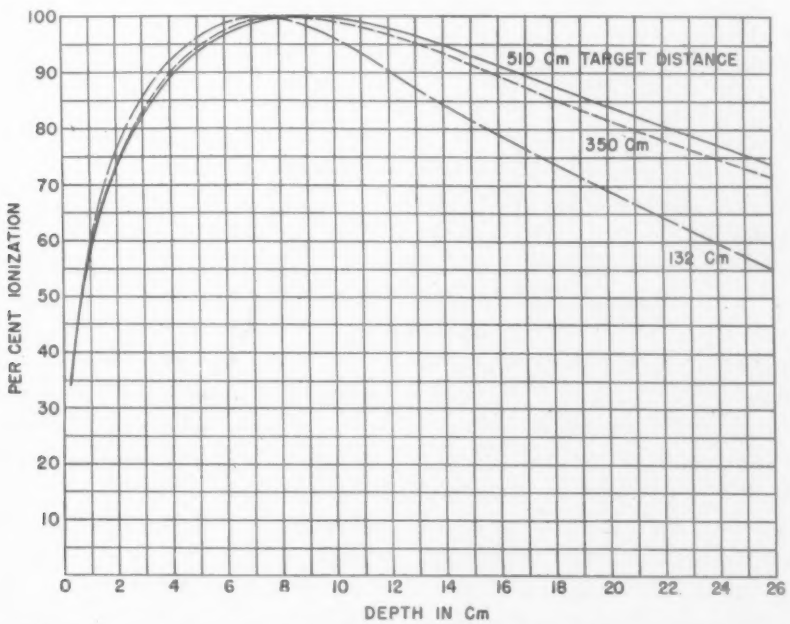


FIG. 14. Effect upon energy absorption of varying the target-phantom distance at 50 mev.

distance from the target to the front of the phantom, then

$$\int_{E}^{E_1} \frac{dE}{E} = \int_{X_1}^{X} \left[-\mu - \frac{2}{X} \right] dx \qquad (1)$$

$$E = E_1 \left(\frac{X_1}{X} \right)^2 e^{-\mu(X - X_1)}. \qquad (2)$$

Thus the radiant flux E incident per unit area at any depth $(X - X_1)$ in the phantom will be equal to the radiant flux incident per unit area on the entrance surface times the inverse square law factor $(X_1/X)^2$ times the absorption factor $e^{-\mu(X - X_1)}$. Since the ionization at any energy and depth is proportional to the primary roentgen-ray beam intensity, any attenuation of the primary beam will cause attenuation of the ionization pattern. This is obscured at depths below the peak, for here as the primary radiation penetrates, it is producing more secondaries and adding them to those previously produced, thus amplifying the ionization. At the peak the secondaries are being absorbed as fast as they are produced, and beyond the peak the decreasing power of the primary roentgen-ray beam to produce ionization becomes apparent. This analysis indicates why the peak and exit ionization varies as it does with target distance at any given energy level. Calculations by equation (2) of the relative exit dose along the axis for different target-phantom distances are found to agree with the experimental value as given on Figure 14 within 2 per cent. From the experimental ionization data as given in Figure 10, one can calculate the ionization intensity at the corresponding depth within the phantom along the axis for different energy levels at any desired target distance. The value of flux E', at a depth $(X' - X_1')$ for any target distance X_1', may be calculated by reading the value of E for the corresponding depth $(X - X_1)$ on Figure 10. For a constant entrance dose the dose E' will vary with position in the phantom according to the equation

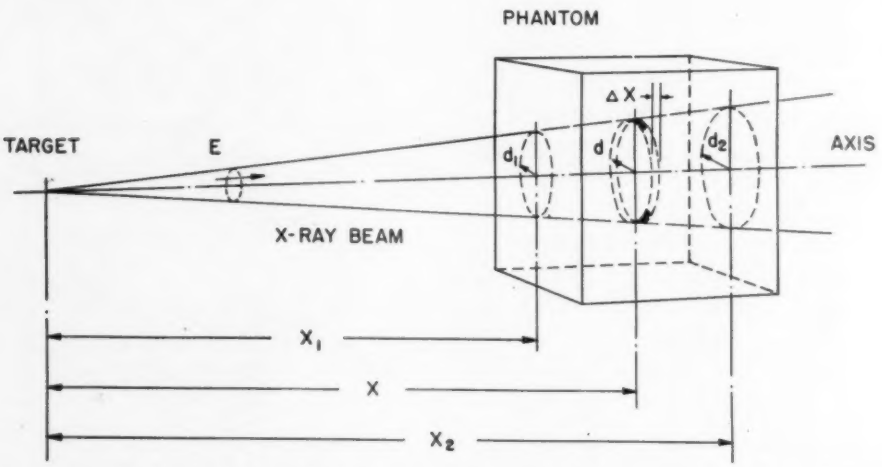


Fig. 15. Schematic diagram for analysis of volume absorption of roentgen-ray beam in phantom.

$$E' = E \frac{\left(\frac{X_1'}{X'} \right)^2}{\left(\frac{X_1}{X} \right)^2} \qquad (3)$$

since the entrance flux and the absorption terms are the same in both cases.

In addition to the ionization intensity, it may be desirable to know the total amount of ionization or total charge produced in a given volume of the phantom. Since no method of doing this by direct experiment was available, the total charge was calculated by integrating the ionization intensity

over the volume. Similar methods of calculation of this total charge have been described by Mayneord[5,6,7,8]. Where the ionization intensity is not known as an explicit function of position, as in the present case, the integration may be approximated by dividing the total volume into small volumes wherein the ionization intensity may be considered constant, and adding the charges produced in each small volume. The effect upon total absorption due to the scattered components, and the field size, has not been included in these calculations. While the effect of scattered radiation plays more of a role at lower roentgen-ray voltages,[9,10] such an omission is of less importance at the higher roentgen-ray voltages for scattering is predominantly forward.

From Figure 15 it is apparent that the total charge generated in the volume of the phantom between X_1 and X_2 will be the sum of the charges generated in volume increments ΔVx. Thus $\mathcal{Q}=\sum_{X_1}^{X_2}\Delta q_x$ where $\mathcal{Q}$ is the total charge. The increment of charge $\Delta q_x=\rho_x\,\Delta V_x$ where ρ_x is the ionization intensity at the depth X, and ΔV_x is the volume of the cylindrical disk of thickness ΔX and diameter d. It is apparent that

$$d=\frac{d_1}{X_1}X,$$

so

$$\Delta V_x=\frac{\pi}{4}\left(\frac{d_1}{X_1}X\right)^2\Delta X$$

and

$$\mathcal{Q}=\sum_{X_1}^{X_2}\rho_x\frac{\pi}{4}\left(\frac{d_1}{X_1}X\right)^2\Delta X.$$

To make the calculation feasible it has been assumed that the beam of roentgen rays passes through a circular aperture which is so constructed and so placed as to produce a conical bundle of roentgen rays 1 cm. in diameter at the entrance skin, across which the roentgen-ray intensity is essentially uniform. Consequently, in the phantom, the volume irradiated will be a frustum of a right circular cone 1 cm. in diameter at the entrance surface, slightly larger at the exit surface, and in this case 26 cm. from entrance to exit. The apex of the cone is at the target 132 cm. from the front of the phantom.

By considering the roentgen-ray intensity to be uniform across the entrance port the calculation will yield the maximum total charge, for actually the intensity falls off as the angle from the axis increases (see Fig. 13). For a distribution range across the field from 100 per cent down to 80 per cent at the edge of the field the total charge values would be reduced by 13 per cent. The maximum total charge separated in the volume of the cone, with the phantom

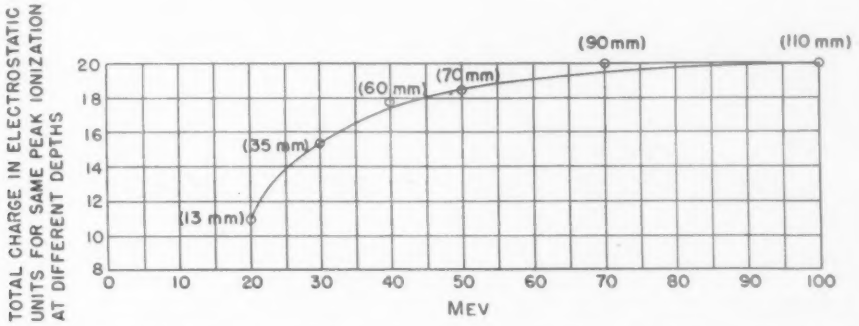
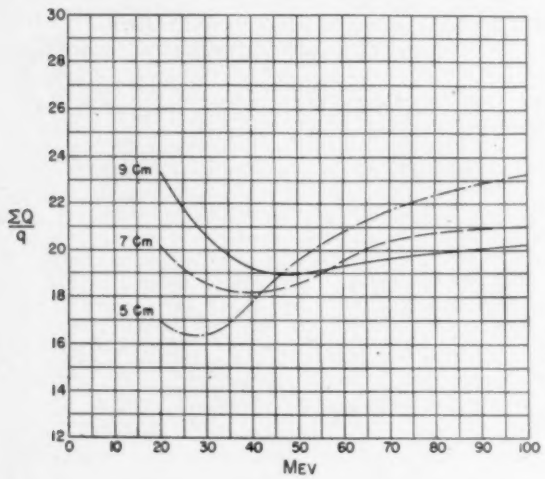


FIG. 16. The total charge in electrostatic units generated in a volume of the phantom 26 cm. deep, 1 cm. diameter at the entrance surface when the maximum ionization density produced in the phantom is 1 electrostatic unit per cubic centimeter. The target distance is 132 cm.

at 132 cm., has been calculated by the above method at 20, 30, 40, 50, 70, 100 mev and the results plotted in Figure 16. At each roentgen-ray voltage the charge has been calculated for the same unit peak ionization intensity as in Figure 10. Thus if the ionization intensity is in statcoulombs/cm³., the total charge will be in statcoulombs, or if it is desired to refer to energy absorbed per unit volume in ergs/cm³., the total energy absorbed will be in ergs.



TOTAL IONIZATION IN PHANTOM PER UNIT INTENSITY AT INDICATED DEPTH

FIG. 17. Total energy absorbed in the conical volume of the phantom to produce unit ionization intensity at the indicated depth.

It is apparent from Figure 16 that if unit peak ionization is considered, the total charge separated in the phantom will increase at higher million electron volts. However, as has been indicated in the discussion of Figures 11 and 12 to obtain unit ionization at a desired depth in the phantom, the peak ionization required decreases as the roentgen-ray voltage increases until the peak occurs at the desired depth. When considering unit ionization at a desired depth these two effects work in opposition, the required peak ionization decreasing with increasing roentgen-ray voltage, while the total charge per unit peak ionization is increasing. To illustrate, Figure 17 has been plotted, showing the total charge separated in the phantom at different roentgen-ray voltages if unit ionization is caused at the depth of 5 or 7 or 9 cm. The values for Figure 17 were calculated in the following manner: (1) By reference to Figure 10 the peak ionization required to produce unit ionization at the desired depth was found for 20, 30, 40, 50, 70, and 100 mev, as was done for Figures 11 and 12. To find the peak ionization required to produce unit ionization at 9 cm. depth using 30 mev. referring to Figure 10, the per cent ionization at 9 cm. on the 30 mev curve is 75 per cent. Therefore, to increase the ionization at 9 cm. from 75 per cent to unity (100 per cent) requires multiplication of the exposure by $\frac{1}{0.75}$ or 1.33 times. This gives an entrance ionization of 40 per cent, peak ionization of 133 per cent, and exit ionization of 50 per cent. (2) Now refer to Figure 16 which indicates that for unit peak ionization the total charge at 30 mev will be 15.5 statcoulombs. Therefore, for a peak ionization of 133 per cent, the total charge will be $1.33 \times 15.5 = 20.6$ statcoulombs. This process, repeated for each million electron volts at several depths, is shown in Figure 17. It indicates that there is an optimum roentgen-ray voltage to produce minimum total energy in the irradiated volume while obtaining maximum energy absorbed at each desired depth. Hence the useful fraction of the total energy absorbed is greater at higher voltages. Ungar[13] has emphasized the importance of maintaining the useful fraction at a high value. Comparison with Figure 10 shows this optimum voltage to correspond closely with the voltage which produces peak ionization at the desired depth.

Filters are of course to be considered when working with the electromagnetic spectrum to reduce the intensity of one wavelength component relative to another. Consequently a filter must have the property of selective absorption, which means that the absorption coefficient of the filter must be different at different wavelengths.

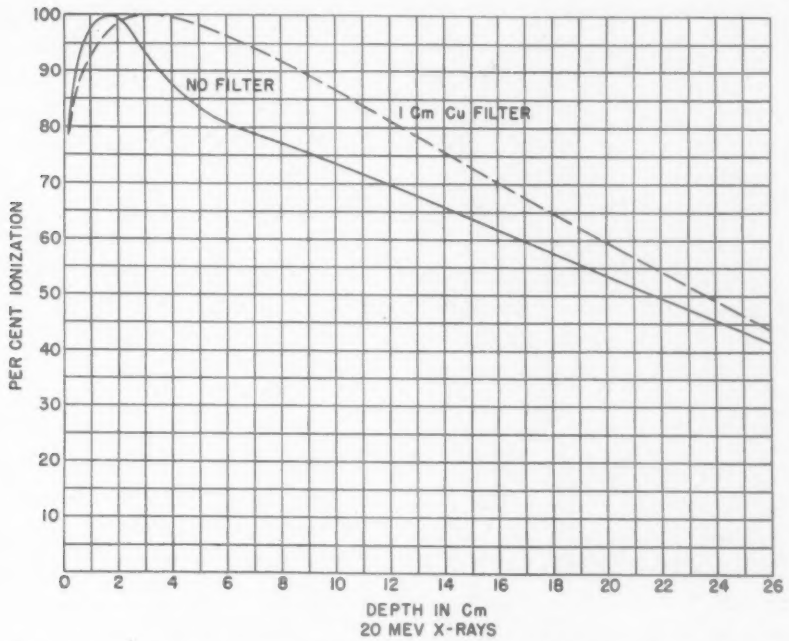


FIG. 18. 20 mev roentgen-ray absorption pattern with copper and with no filter at 196 cm. target-phantom distance.

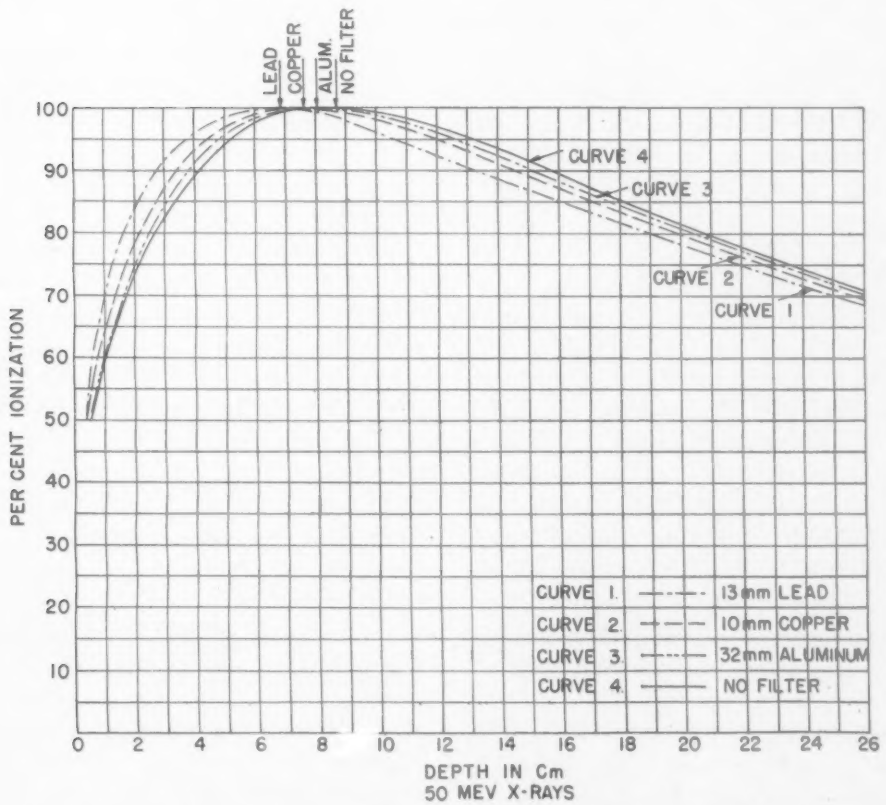


FIG. 19. 50 mev roentgen-ray absorption pattern with lead, copper, aluminum and no filter at 350 cm. target-phantom distance.

Several axial films have been exposed at 20 mev and 50 mev with some filters of lead, copper, and aluminum and the results plotted in Figures 18 and 19, respectively. In doing this work, care was taken to have sufficient space between the filter and the phantom to reduce the screening effect to a low value. This increased the target to entrance skin distance. The copper filter 10 mm. thick used at 20 mev indicates a definite selective absorption of the softer roentgen-ray components and of the spray of electrons emerging from the toroid along with the roentgen rays. The filter experiments with 50 mev were made with lead 13 mm. thick, copper 10 mm. thick and aluminum 32 mm. thick. At 50 mev all of the filters show a slight tendency to soften the radiation, for the peak moves to a lesser depth as it would if lower roentgen-ray voltages were used without a filter. The filter thicknesses in these experiments were chosen to transmit about one-third of the incident radiation. The ineffectiveness of filters at 50 mev was not totally unexpected for previous work on absorption coefficients[14] indicates that the variation of absorption coefficient with wavelength becomes small in this range of roentgen-ray voltages.

IV. CONCLUSION

In conclusion, the depth dose data of these very high energy roentgen rays in a pressboard phantom have clearly indicated that the energy distribution pattern changes very markedly with the large changes in roentgen-ray voltages available. It indicates that there is an optimum roentgen-ray voltage to obtain the maximum ionization intensity at any desired depth. The availability of the great range of roentgen-ray energy levels obtainable from electromagnetic electron accelerators offers the advantages of greater flexibility, enabling one to give maximum ionization at any desired depth, and greater efficiency, giving over a wide range a more favorable ratio of energy absorbed in a particular region to that absorbed in the rest of the volume through which the radiation must pass. The phantom exit absorption may become the limiting factor rather than the entrance absorption in the total dosage problem when applied to therapeutic techniques.

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A NEW PHOTOGRAPHIC MATERIAL FOR GAMMA-RAY DOSIMETRY*

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PHOTOGRAPHIC methods have been used on a routine basis in this laboratory for estimating exposure of personnel to stray gamma and roentgen radiation. Accidents occurring during the handling of fissile materials made it desirable to supplement the standard dental-type roentgen films being used with some other photographic material having the property of being able to record an integrated gamma-ray dose of a higher order of magnitude. Accordingly, a number of commercially available photographic films and papers were investigated in the hope of finding one sufficiently insensitive for the purpose at hand. "Adlux" film, manufactured by the Defender Photo Supply Company, was found to be of the desired degree of sensitivity, as well as to possess unusual uniformity and reproducibility. This film with standard development gives an extreme readable range of densities in the dosage range of 50 to 15,000 gamma-roentgens.

It became apparent that this range includes the range of dosage of therapeutic interest and that the film should therefore prove useful in the measurement of distribution of radiation intensities about multiple radium sources such as are used in therapy. Such measurements made by means of ionization chamber techniques are tedious, while calculations become very laborious or well nigh impossible when more than a few sources or anything but the simplest geometrical arrangements are considered. Film methods have the advantage that a complete three-dimensional plot of radiation intensity about a source or group of sources may be made in a single exposure. In addition, qualitative investigation of the field pattern about a group of sources may be made rapidly and effects of changes in distribution of sources noted. A permanent record is also provided. The degree of precision is not high but is believed adequate for clinical purposes. Film methods in the past have been handicapped to a degree by the limited range of radiation dosage recordable.

I. GENERAL CONSIDERATIONS IN PHOTOGRAPHIC DOSIMETRY

The extension of the international roentgen, originally defined for roentgen rays, to the gamma-ray region has been validated by the work of Gray[4] and others.[7,11] In particular, the conditions under which thimble-chamber measurements are valid as a measurement of dose in terms of the international roentgen have been clarified. The intensity of radiation about a point radium source of 1 millicurie strength and encased in a 0.5 mm. platinum shield, has been determined to be 8.4 r per hour at a distance of 1 centimeter.

Photographic measurements of radiation dose must be calibrated in terms of the primary ionization measurements. There is unfortunately no simple and direct relationship between film blackening and radiation dose. In general, the photographic effect is dependent upon photon energy, the emulsion blackening for unit dose decreasing with increasing photon energy.[1,2,5] There are in addition sharp discontinuities in the curve of specific blackening against

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wavelength in the region of the absorption edges of bromine and silver, at 14 and 25 kv., respectively.[10]

Photographic photometry of visible light has been complicated by failure of the reciprocity law of Bunsen and Roscoe, which defines the exposure as equal to the product of intensity by time and implies that equal exposures should result in equal emulsion blackening. It has been shown by Bell,[1] however, that the photographic effect of a given dose is independent of the dosage rate over a range of roentgen-ray intensities varying by a factor of ten thousand. This point has also been investigated by Morgan.[8]

It is customary to plot the characteristic curve of film in the manner suggested by Hurter and Driffield, namely, density as a function of the logarithm of the dose. When this is done an S-shaped curve is obtained which over a considerable portion of the range approximates a straight line. Bell[1] has also shown that the shape, but not the position, of this curve depends only on the characteristics of the film material and development conditions, and is independent of wavelength.

There are many potential sources of error in photographic methods. Uniform development technique with control of temperature and agitation is of utmost importance in obtaining reproducible results.

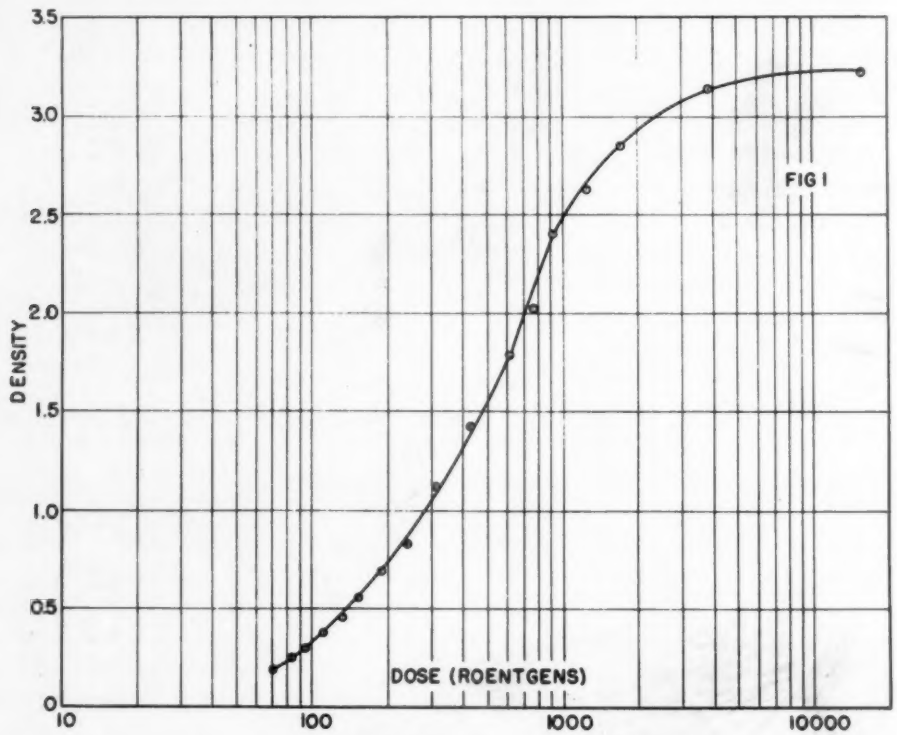

FIG. 1. Characteristic curve of "Adlux" film in air.

Wilsey[10] has discussed in detail the technical requirements that must be met in photographic methods of measurement of roentgen-ray dose.

II. MATERIALS AND METHODS

"Adlux" film consists of a transparent safety base double coated with a bromide type of emulsion similar to that used in projection printing papers. A diffusing medium has been added to the film emulsion, which gives it a translucent appearance. The film is designed for the production of advertising display transparencies. The base stock is 0.015 cm. in thickness,

and the emulsion layers average about 15 microns in thickness. The grain-aggregate size in the developed film varies between approximately 0.5 and 0.7 micron. The film has a matte surface which has incidentally proved useful through the readiness with which notations and construction lines may be made directly on the film. The film was ordinarily handled in the form of 8 by 10 inch sheets.

Tray development in Eastman formula D-72 developer was used. One part of the stock solution was diluted immediately prior to use with two parts of distilled water. Development was carried out at 20° C. for three minutes, with constant agitation. The sheets were passed rapidly but one at a time into a tray containing the developing solution and agitation maintained by repeatedly withdrawing the bottom sheet and replacing it on top of the stack. At the conclusion of the development period the films were quickly transferred to a dilute acetic acid short-stop bath and thence to a standard fixing solution (Eastman Formula F-5). Following complete fixation the films were washed in water and suspended in air to dry. A blank sheet of film was processed with each batch.

Density measurements were made using a "Photovolt" photoelectric densitometer. This instrument incorporates a diffuse illuminating system, phototube and amplifier, with a direct-reading scale calibrated in density units. The primary range of the instrument is from density 0 to 2.0, with provision for extending the range to about 3.2 by resetting the zero point.

The source used in the film calibration studies consists of 500 millicuries of radium bromide, enclosed in a hard-soldered silver cylinder $\frac{5}{8}$ inch in diameter by $\frac{3}{8}$ inch in height. The wall thickness of the container is 1 millimeter. When measurements were made in air using a standard Victoreen condenser r-meter, with 25 r chamber brought approximately to electronic equilibrium by the addition of a plastic cap 3 mm. thick, a radiation dosage rate of 39.0 r per hour was measured at 10 cm. Under phantom conditions a dosage rate of 38.0 r per hour was found at 10 cm. A correction factor of 1.3 has been included as a multiplier of the observed readings to convert to the standard pressure of one atmosphere. The barometric pressure at this location averages 590 mm. of mercury.

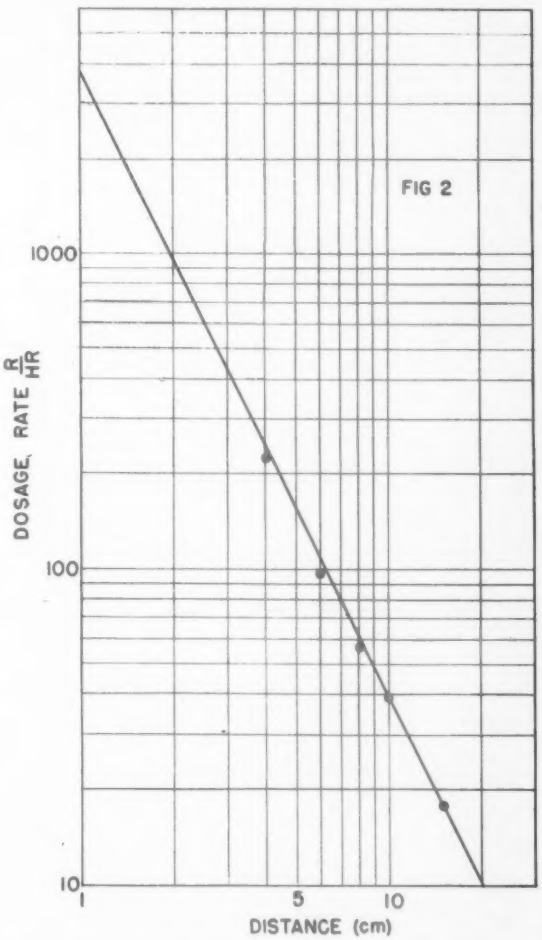

Fig. 2. Inverse-square law curve in air. Circles represent values measured with the ionization chamber, as described in the text.

Film exposures were made both in air and in a phantom of Masonite "Presdwood." For exposures in air the film was enclosed in two thicknesses of black protective paper and it and the source were supported on a thin sheet of cellulose acetate at a distance from any dense scattering material. The phantom was made up of $\frac{1}{4}$ inch slabs of "Presdwood," and was so arranged

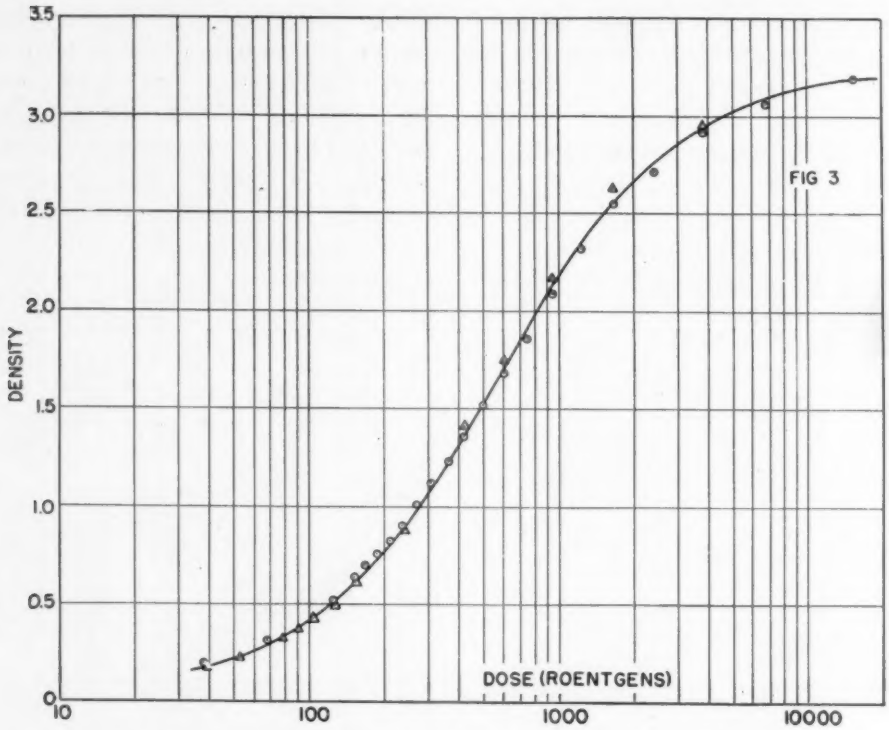

FIG. 3. Characteristic curve of "Adlux" film in "Presdwood" phantom.

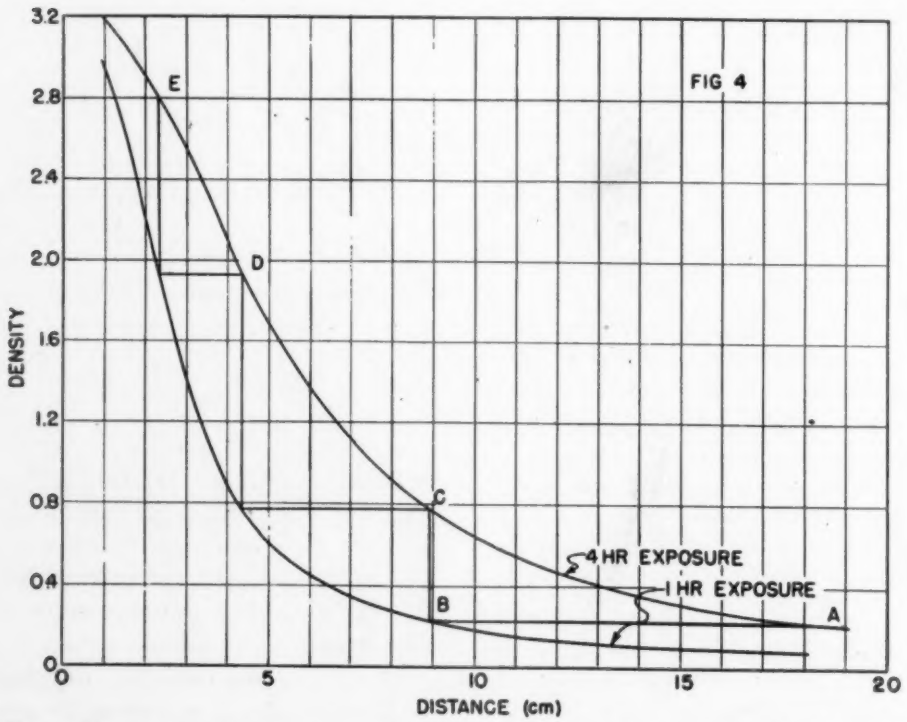

FIG. 4. Density vs. distance curves for one hour and four hour exposures in phantom.

that air spaces were avoided, and the film and source were enclosed on all sides by at least 10 cm. of absorbing material. Reference points on the film were located by pin holes punched in the paper packet enclosing it.

III. RESULTS

Figures 1 and 3 give the characteristic response curves of this emulsion material in air and under phantom conditions respectively.

In determining the response curve in air the inverse-square law was assumed valid for distances rather greater than the physical dimensions of the source. The source was placed at one end of the film packet and a four hour exposure made. The film was then processed and its density at various distances from the center of the source measured. In Figure 2 the computed dose rate against distance curve is shown together with the values measured by the thimble chamber. From this and the observed density against distance relationship the density against logarithm of exposure curve in Figure 1 was drawn.

Figure 3 shows the similar response curve under phantom conditions. Here no assumptions were made concerning the form of the radiation field surrounding the source. One hour and four hour exposures were made and density against distance relationships are plotted in Figure 4. It is apparent that any horizontal line drawn on this chart cuts the two curves at points of equal density and hence, assuming the reciprocity law valid, at points of equal radiation dose; while any vertical line cuts the two curves at points where the dosages are in the ratio of four to one. Hence, if point A be assumed to correspond to a dose of one unit, point B received this same dose and point C, four units. Similarly, point D received sixteen units and point E, sixty-four units. The log-log plot in Figure 5 shows no significant deviation from the straight line of slope -2 predicted by the inverse-square law out to a distance of 19 cm., fitted to the experimentally determined value of 38 r per hour at 10 cm. On this same plot are shown the dosage rates determined by the thimble chamber at various distances. From it the density against log exposure curve in Figure 3 was determined. The circles enclose points determined from the one hour, and the triangles, points from the four hour exposure.

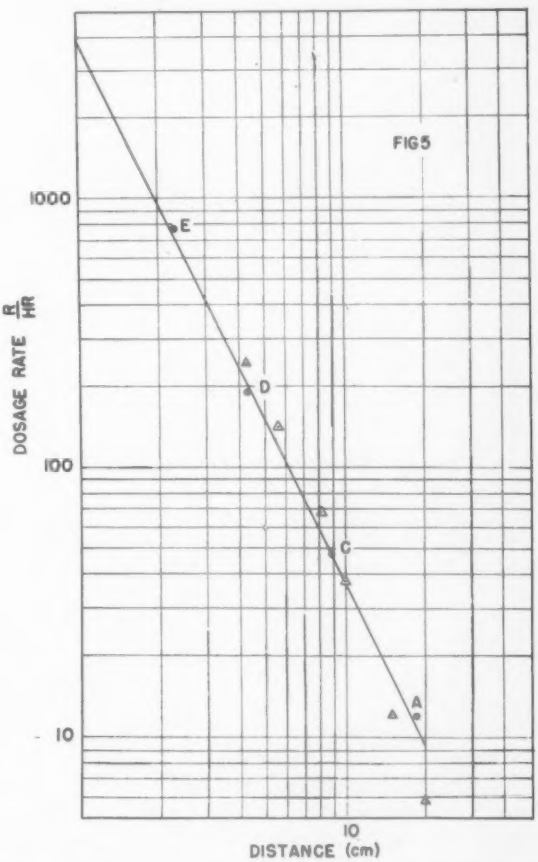

Fig. 5. Distance vs. dose in phantom. *Solid line:* inverse square law. *Circles:* values by film measurement. *Triangles:* values by ionization chamber.

A final experiment was performed to show the ability of the film to record the radiation field about multiple sources such as might be used in gamma-ray therapy. The arrangement chosen for investigation was that of three linear sources in a tandem arrangement. Actually a single source (NBS No. 13078) was used and was moved successively to its two new positions during the exposure. This source contains 9.92

milligrams of radium in a platinum needle 0.5 mm. in wall thickness and 1.75 cm. in length. Its active length is 1.5 cm. In the figure (Fig. 6) three sets of isodose curves are drawn: (1) the experimentally determined set; (2) calculated isodose curves

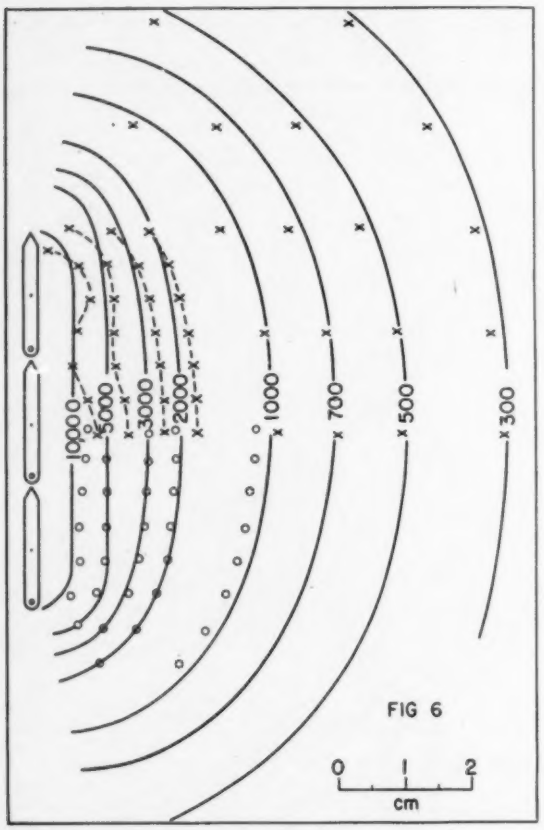

FIG. 6. Dosage rates about tandem (see text). *Solid lines:* photographic method. *Circles:* Quimby's data. *Crosses:* approximate calculation (see text).

from the data given by Quimby[9] for a uniform source of 5 cm. length; and (3) calculated curves determined by replacing each source by an equivalent point source at its geometrical center and adding the contributions of each at each point of interest. It is seen that there is substantially good agreement between the experimental and the calculated curves.

In all such measurements it is absolutely essential for accurate results that a calibration film and a blank be processed with each batch.

IV. DISCUSSION

It is surprising to note that this film method shows such close agreement with the inverse square law out to such large distances (approximately 20 cm.) in the phantom. At such distances, differences due to absorption are large and are readily measurable when an ionization chamber is used. The agreement is purely fortuitous and must be due to an increased sensitivity of the film to scattered radiation of longer wavelength. However, there is good agreement with ionization chamber measurements out to distances (approximately 10 cm.) which are likely to be of clinical interest.

Investigation of the response of this film to a wide range of photon energies (50 kv. to 20 mev.) is under way, and will be reported in the future. Preliminary work indicates that there is no significant difference in the response of the film to the primary radiation of radium, which has an average energy of 0.7 mev., with photon energies ranging from 0.3 to 2.5 mev., on the one hand, and to the gamma radiation from Co^{60} which has well defined photon energies of 1.1 and 1.3 mev.

V. CONCLUSIONS

Gamma-ray dosimetry with the aid of a special, commercially available film has been discussed. This film has been shown to have unusual latitude and reproducibility. Characteristic curves for this material both in air and under phantom conditions are presented. The use of this material for investigation of the radiation field about complex arrays of sources is feasible and the method is capable of giving results well within clinical tolerances of accuracy.

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SOME CONSIDERATIONS IN THE TREATMENT OF HEMANGIOMA IN INFANTS AND YOUNG CHILDREN*

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HEMANGIOMA of the skin or mucous membrane is a lesion familiar to every doctor. It is a benign vascular tumor which should receive treatment because of the cosmetic deformity or because it interferes with function. The condition is congenital and the most important thing about the lesion is that whatever treatment is given should be given early, that is, as soon after birth of the infant as possible, or as soon as the blemish appears.

FIG. 1. Photomicrograph showing marked cellularity in a hemangioma. The endothelial channels are numerous and many of them do not contain blood. This type of lesion is thought to be capable of further growth. Clinically a lesion of this type is indistinguishable from a less cellular lesion. (Microscopic slide loaned by Dr. Robert C. Horn, Surgical Pathologist, Hospital of the University of Pennsylvania.)

A hemangioma is a localized hyperplasia of the cutaneous or subcutaneous vascular tissue. The lesions may involve the dermis, the subcutaneous tissue, or both. They range greatly in size, are reddish or purplish in color, with a flattened surface, which is on a level with the skin or slightly elevated above the general level.

Growth of hemangiomas is thought to be accomplished by budding of vascular channels and proliferation of endothelial cells. In some of these lesions, proliferation becomes a major consideration (Fig. 1).

Vascular nevi may be separated on an anatomic basis into three groups[11] (1) flat or slightly elevated tumors composed of a superficial plexus of dilated capillaries, angioma simplex, naevus flammeus; port-wine stain; (2) hypertrophic angiomas, made up of an interlacing network of blood vessels of considerable size, angioma plexiforme; angioma simplex hyperplasticum; and (3) cavernous hemangiomas.

The simple angioma, as a rule, appears shortly after birth.

The "port-wine stain," or *naevus flammeus*, occurs as several varieties. Experience with Chaoul roentgen therapy in treating pink lesions in the very young is most encouraging. The deeply colored lesions are helped only slightly. The skin is thin in this type of lesion, and the vessels are thin walled and superficial, situated immediately beneath the epidermis. The endo-

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thelial lining of the vessel walls is quite thin and thought by some to be radioresistant because of its mature adult type of endothelium[12] (Fig. 2).

The *hypertrophic vascular nevi* and the *cavernous hemangiomas* may be discussed together. They are more or less elevated with a nodular or lobulated surface. The tumors vary in size and color, are soft and compressible. Swelling of the lesion can be produced or increased by gravity, exertion

Fig. 2. Photomicrograph of a "port-wine stain." Numerous vascular channels with mature adult type endothelium are seen just beneath the epidermis. (Microscopic slide loaned by Dr. Herman Beerman, Assistant Professor of Dermatology, University of Pennsylvania.)

or crying. The lesion may ulcerate or rupture and may produce severe hemorrhage. The lesions develop slowly and may cause serious alteration, hypertrophy, or destruction of the tissues by altering the blood supply. They may occur anywhere.

The lesion may be composed of thin-walled dilated capillaries, having a single afferent vessel, or it may have many of the larger vascular components such as arterioles and small arteries and veins (Fig. 3, 4 and 5). The results in treating these lesions (strawberry mark) are gratifying.

THERAPEUTIC CONSIDERATIONS

Over the years, a great many physicians have elected not to recommend treatment

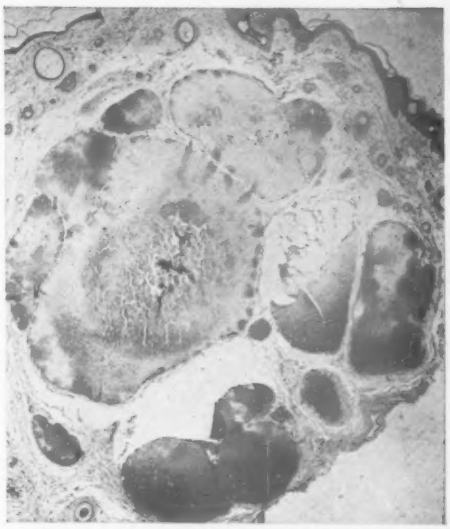

Fig. 3. Photomicrograph of a naevus vasculosis or "strawberry mark" showing blood-filled dilated capillaries. This type of lesion responds well to treatment. It will blanch readily on light diascopic pressure. (Microscopic slide loaned by Dr. Robert C. Horn, Surgical Pathologist, Hospital of the University of Pennsylvania.)

Fig. 4. Photomicrograph showing a cavernous hemangioma which contains arterioles, venules, and small arteries. (Microscopic slide loaned by Dr. Herman Beerman, Assistant Professor of Dermatology, University of Pennsylvania.)

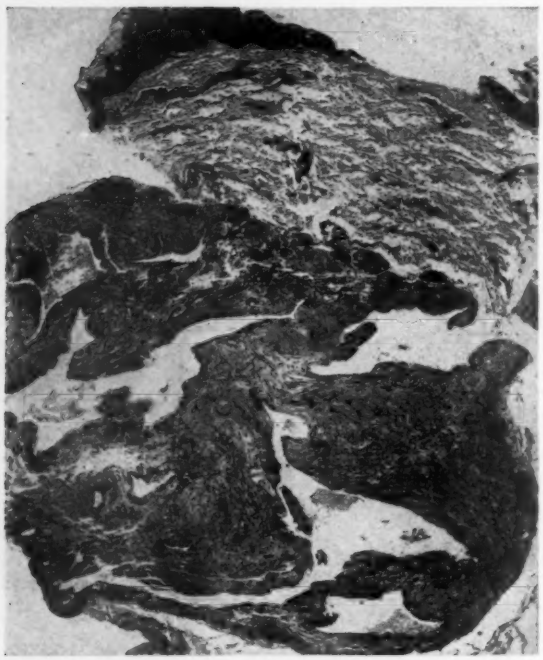

FIG. 5. Photomicrograph showing large veins found in some of the cavernous hemangiomas. This type of lesion is more resistant to treatment by roentgen rays and radium. (Microscopic slide loaned by Dr. Robert C. Horn, Surgical Pathologist, Hospital of the University of Pennsylvania.)

for cavernous hemangiomas, largely because they have been taught that most of the hemangiomas will disappear spontaneously. Indeed, Lister,[4] in 1938, states that he observed 77 patients for seven years, and in that group, over one-half of the angiomas disappeared completely and in the other half the lesions stopped growing and showed evidence of retrogression. Nancel-Pénard[5] and Winer[13] are in agreement with the views expressed by Lister.

While preparing this article, one of us received the following letter:

> . . . It is mildly depressing to me to learn that another paper on the radiation treatment of hemangiomas is going to be written when even the immediate results by radiation are inferior to CO_2 snow.
>
> One has to treat hundreds of patients and live fifteen or twenty years to see the twisted faces, short arms and legs, and small hands to realize how unjustifiable the method is. Can't you possibly read a paper about anything else?

The writer of this letter, a distinguished member of this Society, perhaps is not alone in his belief and there are those who are in complete sympathy with his views. To us, this is a challenge. We believe that hemangiomas can be treated with radiation with complete satisfaction. The poor results that encourage statements like the above can be avoided if a little common sense is used in planning the treatment. We know this because we have observed our results over a period of twenty years and in no instance have we obtained unsatisfactory results that can be attributed to irradiation.

There is no doubt that some of the lesions do heal spontaneously, but it is not possible to predict with assurance which lesions will remain quiescent, grow or disappear spontaneously. Even if it were known that 50 per cent or more of the lesions would disappear, we still would recommend irradiation for the following reasons: (1) radiation can be administered without harmful effects; (2) small doses of radiation will enhance any natural tendency of the lesion to disappear; (3) the results are excellent and are superior to any other method that we have observed. A physician has no right to deny treatment to a patient because of the hope that the lesion will disappear without treatment.

We have seen many hemangiomas in adults, many on the faces of young women, who when the histories were taken, stated that their parents were advised by the family physician, and often by a dermatologist, that treatment should be deferred until the baby was older or that the condition would disappear without treatment. Such advice, we believe, will lead many times to tragic situations, especially in girls.

The methods of therapy for the various types of hemangioma by others include: (1) surgical excision; (2) roentgen therapy; (3) radium therapy; (4) grenz rays; (5) carbon dioxide snow; (6) injection of sclerosing solutions; (7) tattooing (Conway and Docktor[2]); (8) ultraviolet radiation under pressure; (9) electrocoagulation, and (10) cosmetic disguise.

For many years we used radium needles, molds and plaques in the treatment of cavernous hemangiomas. It is a commendable form of therapy and many excellent results were obtained. Since 1937, when Chaoul equipment was acquired by us through the generosity of Mr. William H. Donner, we have used contact roentgen therapy in place of topical radium, and we have been pleased with our results. Our comments in this presentation will be limited to a discussion of contact roentgen therapy, 100 to 140 kv. intermediate roentgen therapy and radon implantation in certain hemangiomas.

Our experience since 1938 consists of the treatment of 560 hemangiomas in 406 patients. The distribution of these lesions is illustrated in Chart 1.

We wish to emphasize at this point, and we will emphasize it again, that hemangiomas are most effectively treated when the patient is seen early, and by early we mean the first few weeks of life. We do not believe in watchful waiting. A hemangioma treated at three weeks of age requires less treatment and responds better than one treated at three months.

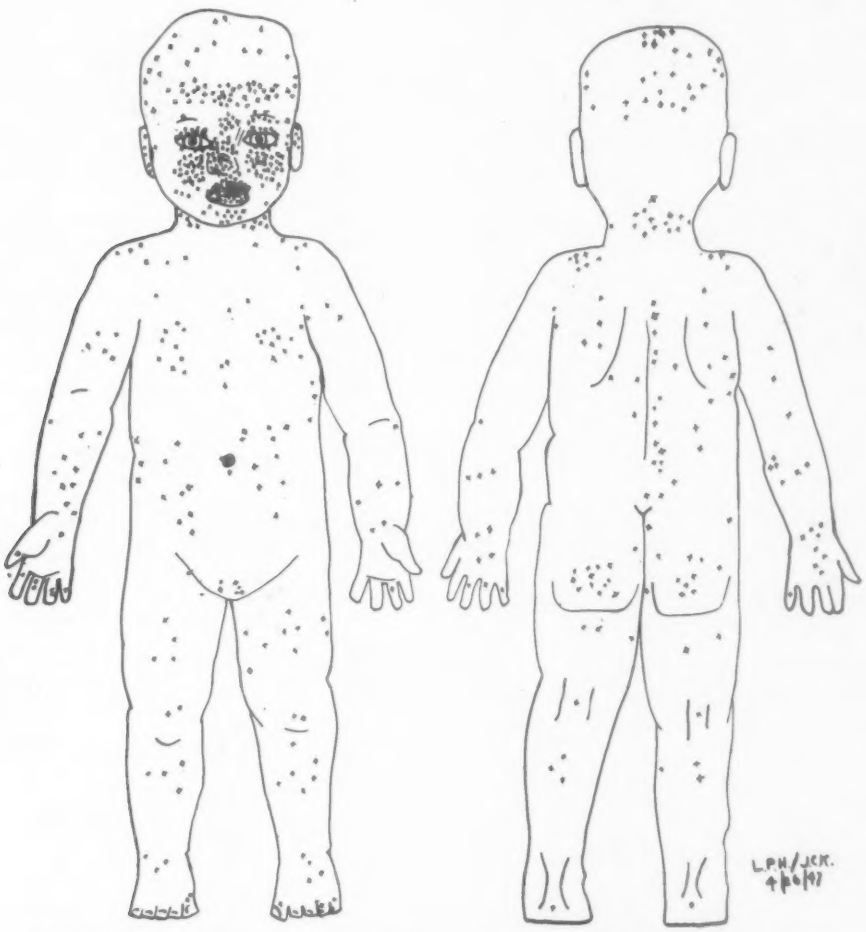

CHART 1. Distribution of 560 hemangiomas in 406 patients treated since 1938 by contact therapy and/or interstitial radon tubes.

In general, the technique we employ may be divided into two parts: (*a*) control of the superficial or dermal elements by roentgen therapy, and this part should be done first, and (*b*) control of the deeper portions of the lesion by implantation with radon seeds or

use of intermediate voltage therapy. The best cosmetic effect is obtained when the superficial portions of the lesion are treated very early. The earlier this portion of the lesion is treated, the better the result. In general, the lesions which respond best are those which easily blanch with light diascopic pressure. They are the lesions with the small vascular channels just beneath the skin, and are easily obliterated by irradiation.

FIG. 6. Sample finger nail polish scale furnished by Cutex. Accurate color matching is possible when these scales are used and minute changes are noted in the treated hemangiomas at the time of each visit. These color charts may be obtained from the finger nail polish manufacturers.

At the time of the first visit, the patient is given a general physical examination. The contour of the hemangioma is traced upon a piece of transparent paper and its measurements are recorded. Color photographs are made. The color of the lesion is recorded, having been matched with a color on one of the finger nail polish scales by the parents and by the radiologist (Fig. 6). The treatment that we recommend is given over a period of months. The anticipated changes (flattening of the lesion, loss of original color and appearance of white skin) are explained to the parents. The change occurs so slowly parents may overlook them until the comparative colors illustrate the gradual skin blanching. These small details have assisted in preventing impatience on the part of the parents. The lesion is tested for blanching with diascopic pressure. If the lesion is not completely blanched by pressure the prognosis for complete disappearance should be guarded. Changes in size or color are noted when the patient is inverted and during crying. If the lesion is situated over some epiphyseal center or closely over any growing bone, a roentgenogram is made of the area and, if it is an extremity, a roentgenogram of the normal opposite extremity is made. Irradiation can disturb the growth of bone; therefore, one should explain such possibilities to the parents. We have had

FIG. 7. Roentgenograms made at three and eight years. The patient received 900 r to multiple portals over the right hand on the palm and dorsum at the age of three months. There has been no injury to the bones and no retardation of growth attributable to the irradiation. Many patients have been followed for longer periods than this and have received more treatment without bony change.

no such complications and they are not likely with the method that we employ (Fig. 7). We have observed many instances of overgrowth of bones due directly to untreated hemangiomas, a fact which

.....194.....

In consideration of Dr. E. P. Pendergrass, or any of his associates (radiologists), undertaking the case of

.....who has been referred to

us by.....for the treatment of

.....the undersigned understands that in attempting to treat the condition from which he suffers it may be necessary to do permanent injury to the skin, such as secondary ulceration, telangiectasis (prominent blood vessels), or permanent tanning. The condition from which the undersigned suffers has been fully explained and he (or she) hereby gives his consent, without any reservation, to undergo such treatment as may be directed by the radiologist in charge.

Signed:.....

Witness:..... Relative:.....

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In consideration of Dr. Eugene P. Pendergrass, or any of his associates (radiologists), undertaking the case of

.....who has been referred to

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.....the undersigned understands that it is necessary to treat over the skull, and in doing so the x-ray or radium treatment may remove temporarily, or permanently, the hair. The undersigned agrees without any reservations to undergo such treatment as may be directed by the radiologist in charge.

Signed:.....

Witness:..... Relative:.....

Form 502

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In consideration of Dr. Eugene P. Pendergrass, or any of his associates (radiologists,) undertaking the case of

.....who has been referred to

us by.....for the treatment of

.....the undersigned understands that in treating lesions around the eye an effort is made to protect the eyeball from direct irradiation. Often this is impossible due to the position of the lesion, and it is almost impossible to protect it from secondary irradiation. Irradiation may cause cataract formation, or it may cause a disturbance in the vision by direct effect upon the retina, or it may cause telangiectasis, or it may cause a removal of the eyelashes, which may be permanent. All of the above possibilities have been carefully explained to the undersigned, who hereby gives consent for such treatment as may be directed by the radiologist in charge, without any reservation.

Signed:.....

Witness:..... Relative:.....

505-6

FIG. 8. Sample cards which parents are asked to sign before treatment is given.

also should be explained to the families of the patient, especially by those who do not recommend irradiation.

It is well to tell the parents that occasionally the large boggy hemangioma may break down and "slough." If sloughing occurs following treatment, the family and referring doctor are likely to attribute the destruction of tissue to the irradiation. We have seen more sloughing hemangiomas occur without irradiation than with it. Nevertheless, such a possibility is explained to every patient. We are sure that such practice will obviate mediolegal complications. In our experience, sloughing has occurred only in the large bulky and boggy lesions. Sloughing areas always heal, but leave white scars. They must be cared for to prevent secondary infection.

When lesions occur on the scalp or around the eyes, the family is advised about the possibility of hair falling out and not returning. The parents are asked to give a signed permission before treatment is begun (Fig. 8). Likewise, radon implanted into the orbit might injure the eye. We tell the family of such possibilities and ask for signed permission before proceeding with the treatment. Thus far, we have had no eye injuries and only one patient in which the eyelashes failed to return. There is no danger to the brain in treating hemangiomas of the scalp with the method to be described. In certain large hemangiomas which involve the face and scalp unilaterally, the hemangioma may extend into the brain and lead ultimately to hemiatrophy. Roentgenograms of the skull are obtained in such instances and at frequent intervals. The family are completely informed about the possibility of hemiatrophy of the brain before treatment is instituted. In the few cases of this type that have been treated no untoward results have occurred. Even the hair has not been destroyed.

Isodose curves for the Chaoul roentgen therapy unit have been persented in previous papers with other physical data.[1,6,7,8,10] Quimby and Focht have reported isodose data on the Philips unit.[3,9] The depth dose of these radiations parallels quite closely that of radium (Fig. 9).

We believe contact therapy offers the following advantages over topical radium: (1) there is danger to the operator in the handling of radium over a period of many years in the preparation and application of plaques and molds; (2) application of Chaoul therapy requires a much shorter

period of time than does radium; (3) the distribution of the radiation from the Chaoul unit and a well prepared radium plaque are about the same; (4) there is much less difficulty in holding the patient quiet for the short time required for the close distance roentgen therapy; there is less difficulty in treating certain areas with the Chaoul and the Philips therapy units such as those occurring on the lips, eyelids, scalp, vagina, etc.; (5) the skin end-results seem

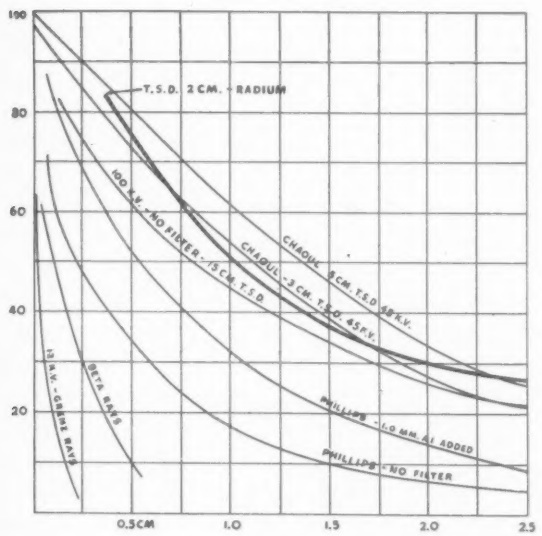

FIG. 9. Absorption curves for the qualities of radiation which are employed. The similarity of radium and contact roentgen therapy is illustrated.

better with roentgen radiation than with radium.

If the lesion is small and is located either around the eye, the lips or the nose, we prefer to use the Philips unit because it is easier to protect the eye, the eyebrow, and the eyelashes because of the greater latitude in dosage output per minute and the adaptability and sizes of the available cones. We use the Philips unit in certain other areas such as the labia where it seems more adaptable. In every other situation we prefer to use the Chaoul apparatus. The number of portals used depends upon the size of the lesion and its shape. The skin-target distance depends upon the depth of the lesion. In the port-wine stains, we would prefer to use the 1.9 cm. distance available with the Philips unit. In the deeper or thicker lesions 3 to 5 cm. skin-target distance is used with the Chaoul unit. In certain instances where the lesion is particularly large and bulky we employ intermediate voltage 75 to 135 kv. Most of the small and deep-seated hemangiomas are treated with radon after the skin discolora-

Kv.	*Added Filtration*	*Half-Value Layer*
44 (Philips)	None	0.3 mm. Al
44 (Philips)	2.5 mm. Al	1.4 mm. Al
45 (Chaoul)	None*	2.4 mm. Al
75	None**	0.6 mm. Al
75	1 mm. Al	1.7 mm. Al
75	2 mm. Al	2.3 mm. Al
75	3 mm. Al	2.5 mm. Al
100	None**	0.8 mm. Al
100	1 mm. Al	2.2 mm. Al
100	2 mm. Al	2.8 mm. Al
100	3 mm. Al	3.1 mm. Al
135	None**	1.2 mm. Al
135	1 mm. Al	2.5 mm. Al
135	2 mm. Al	4.0 mm. Al
135	3 mm. Al	4.6 mm. Al
135	5 mm. Al	5.0 mm. Al†
135	1 mm. Al plus 0.25 mm. Cu	9.0 mm. Al†

* Inherent filtration 0.2 mm. nickel.
** Inherent filtration about 0.2 mm. Al.
† Estimated values.

FIG. 10. Illustrating the quality of the types of radiation employed.

tion has been removed by roentgen therapy. With intermediate voltage we use 1 to 3 mm. aluminum filtration with half-value layer of 2.4 to 4.6 mm. Al; the filtration of the radiation with the Philips and Chaoul units ranges from unfiltered to 0.2 mm. nickel. The half-value layer of the radiation is 2.4 mm. aluminum[7] with the Chaoul apparatus and 0.3 mm. aluminum with the Philips unit at contact[9] (Fig. 10).

In preparing the patient for treatment he is restrained by wrapping securely with a small sheet (Fig. 11). Sand bags are useful in the younger children and will often serve as adequate restraint for the lower extremity. The area being treated is held by the radiologist or his assistant (properly

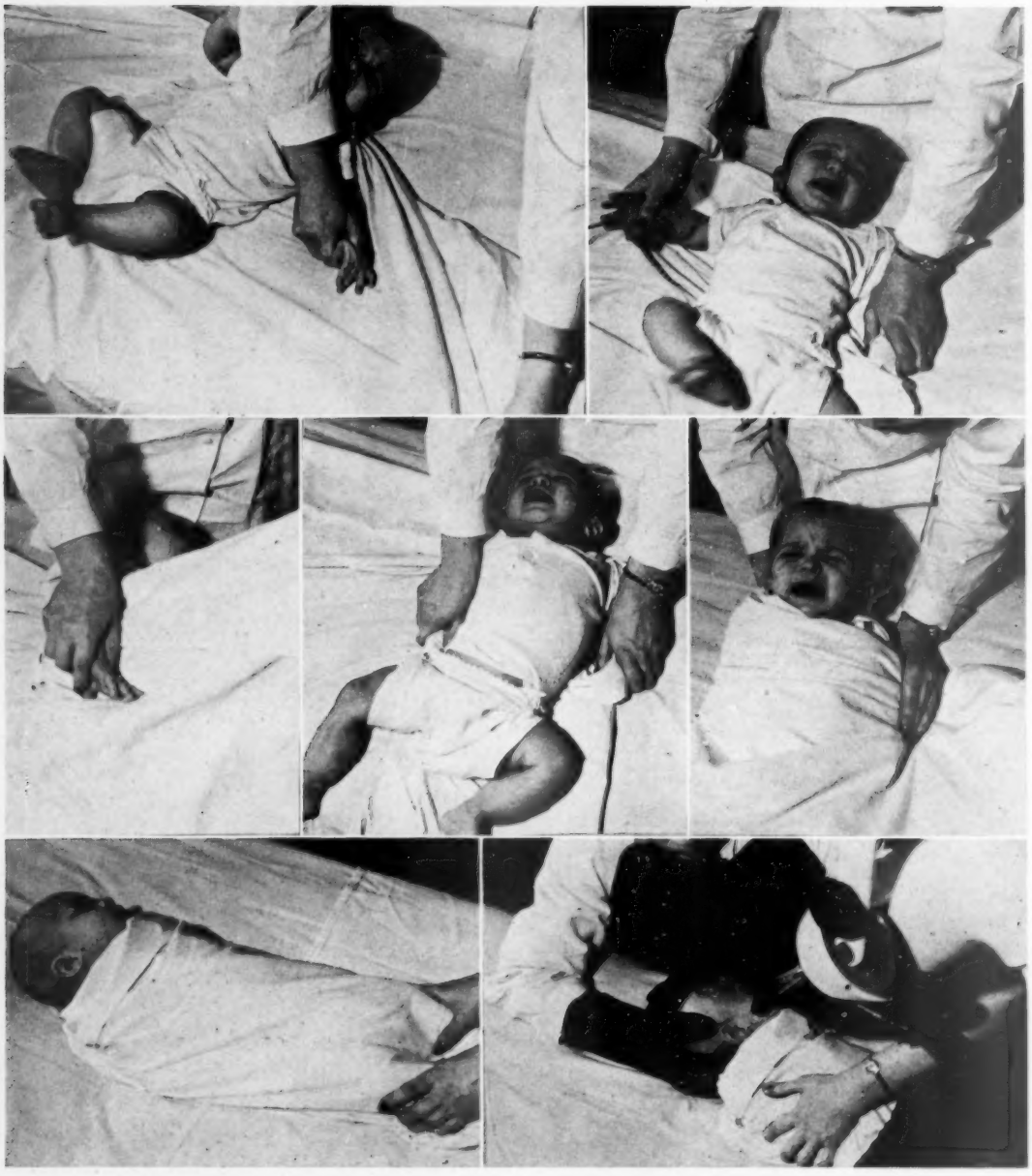

FIG. 11. Steps employed in wrapping the infant in order to restrain it during treatment. The radiologist or his assistant, adequately protected, firmly holds the area to be treated against the treatment cone. Sand bags are frequently used and the infant's parents are asked to help.

protected) and the part is held firmly against the treatment cone (pressure and counterpressure (Fig. 11). Additional restraint is furnished by the parent and this is particularly useful in older children. When a relatively large treatment cone is used we have found it helpful to *cover the end of the cone with scotch tape* to press the central portion of the lesion flat to the rest of the lesion. Otherwise, in very small lesions, the central portion may extend up into the treatment cone where it will get considerably more treatment because distances of a few millimeters are quite important. The lesion is then given 200 to 400 roentgens (as measured in air) through as

many portals as are required to cover it. It is not necessary that these portals overlap. If the portals approach each other as closely as 1 to 2 mm. the effect is adequate are required and usually less than 1,500 r is given. Actually 75 per cent of our patients treated with Chaoul therapy only received less than 1,250 r, and 95 per cent received

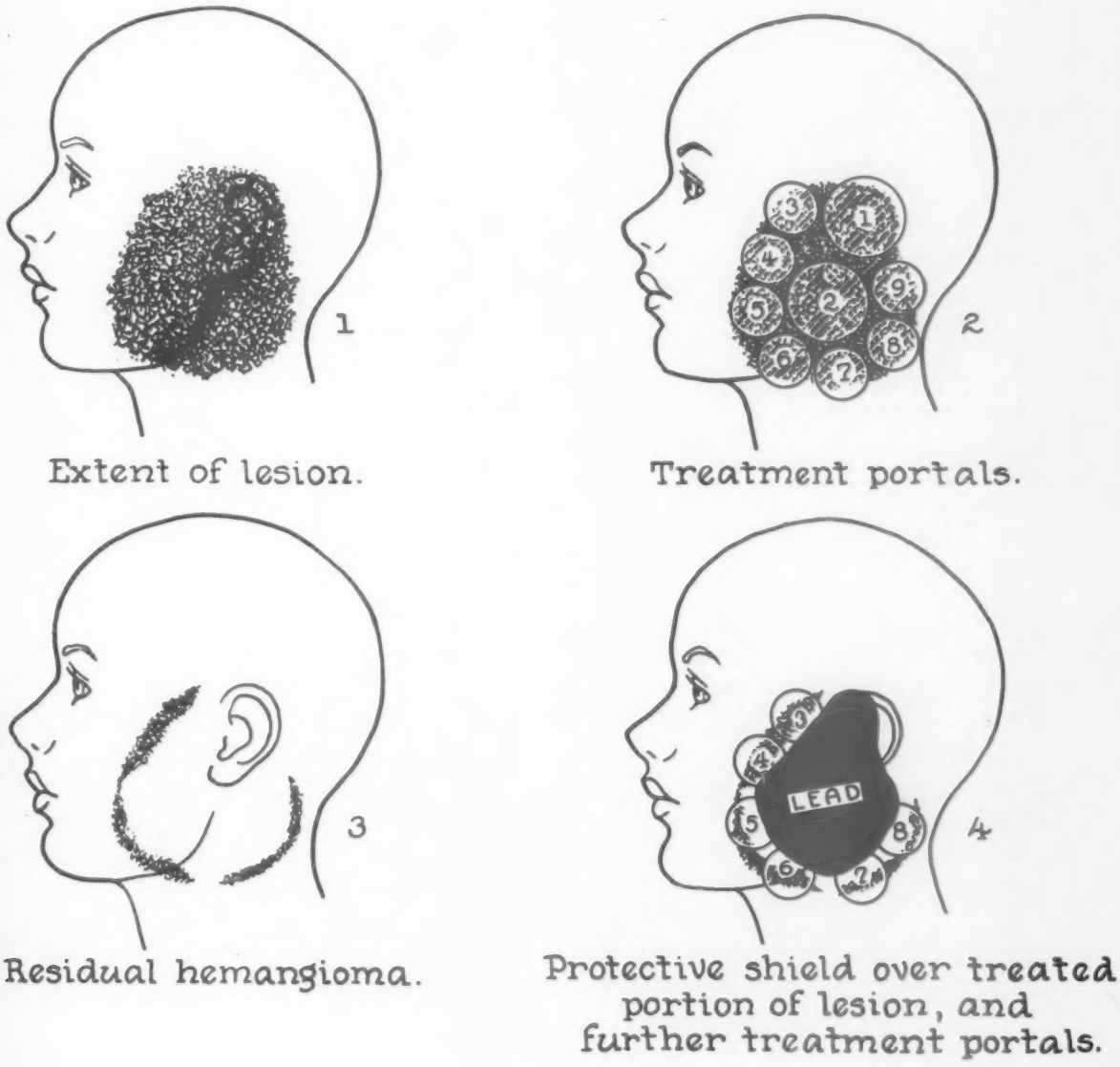

FIG. 12. Showing plan of treatment through multiple portals to a large lesion on the left cheek. It is not necessary that the portals overlap.

(Fig. 12). The patient is seen at intervals of four to six weeks. If no trouble is anticipated (such as possibility of sloughing, etc.) and the patient lives at a considerable distance, 400 r or rarely even more, may be given and the patient seen in three months. Usually three to seven treatments (visits) less than 1,750 r, the treatment time extending over a period of eighteen months.

In treating lesions on the face or other parts of the body where a normal appearing skin is desired, the dosage should be small and given very slowly. If large doses (500 r) are employed the skin effects will simulate

those of a faint vaccination scar. Lesions on parts of the body that are not exposed are treated enough to stop their growth. Under such circumstances, one to three treatments as a rule, are all that are necessary.

The more deeply situated portions of the hemangioma are treated with implantation of radon seeds of 0.1 to 0.5 mc. strength. We prefer to use small seeds implanted through multiple punctures. This technique will prevent migration of the seeds resulting in faulty distribution due to the "massage effect" often seen when all seeds are implanted through a single opening in a movable part such as the cheek or eyelid. For a lesion 1 cm. in diameter usually one seed 0.25 to 0.5 mg. in strength, will be implanted. If such a dosage does not produce an adequate response another seed may be implanted at a later date. We prefer to err on the side of too little treatment rather than too much. One thousand gamma roentgens delivered to the lesion is usually adequate.

In general, all lesions respond well if treated early. In some small bluish-red lesions, when it is presumed that the large venous elements are in preponderance, the family is advised that it will take a longer time to obtain a good result.

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COLLOIDAL LEAD ORTHOPHOSPHATE ASSOCIATED WITH DEEP ROENTGEN THERAPY IN BONE METASTASES FROM CANCER OF THE BREAST*†

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FOR the past forty-five years repeated attempts have been made to use metallic substances for the treatment of cancer. Colloidal solutions of gold, copper, silver, bismuth, arsenic, sulphur, selenium and a variety of other elements or their compounds have been tried in turn, only to be discarded because of the indifferent success obtained by their use.[14,34,42,43] During the time of World War I, Bell,[6–11] after noting the rather slow rate of growth of cancer in lead workers, and based on the long known fact that lead causes abortion in pregnant women, carried out a series of experiments with this substance in growing plants and animals.

Bell used metallic lead which he suspended in a number of rather imperfect colloidal solutions. As he states, the whole object of the colloidal preparation was to deliver the lead to the highest bidder, as it were, among the body tissues without producing too many deleterious effects generally. Whereas a dose of little more than 0.2 gram of soluble lead was considered fatal when given in a single dose, with the suspended solutions it was possible to give 0.6 gram in seven or eight doses during a period of four months and have no serious consequences develop. The preparation of a suitable colloid, however, continued to represent a major problem. In the later phase of the work Bell used an electrical suspension of the metallic lead in an aqueous medium with a small amount of gelatin and calcium chloride, but even so the poor keeping qualities of the solution prevented a more general use of this form of chemotherapy. Bell himself repeatedly emphasized that the method is difficult and to some extent dangerous and that it can only be safely employed by those who have proper laboratory facilities at their immediate disposal.

Concerning the biologic effect, Bell found that the metallic lead has at least two attributes: (1) it has the power to arrest cell growth in general; (2) it has a certain special affinity for the chorionic epithelium and the malignant cells. The general arrest of cell growth was observed experimentally in all young plants and animals under investigation. The affinity for the chorionic epithelium manifested itself in the form of coagulation necrosis leading to abortion. The chemotherapeutic index of this effect was estimated as being approximately two. Under favorable circumstances a similar necrosis induced by the metallic lead was observed also in the cancer cells, although the chemotherapeutic index here was somewhat lower.

In 1926 Bell published the clinical results obtained in the treatment of a series of 200 cases of cancer. He arrived at the conclusion that all types of malignant neoplasms are probably amenable to the beneficial influence of lead, provided the metal can reach the tumor cells in sufficient quantities. Adjuvant surgical and radiation measures were considered to be of great aid in suitable circumstances. Finally, he anticipated that the effects of irradiation would be augmented by the previous use of lead.

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The observations made by Bell were borne out to a certain extent by Wood,[43] who also experimented with colloidal solutions of selenium, sulphur, silver and copper. Wood noted that the effect of lead on the tumor is characterized by intense congestion, thrombi formation in the capillaries twenty-four hours later, necrosis and finally absorption and shrinkage of the tumor. In using lead combined with deep roentgen therapy he found that the partial poisoning of the cancer cells by the metal and the injury produced by the roentgen rays add up, leading to an enhanced therapeutic effect.

Following this report of Wood and impressed by the investigations of Bell, Ullmann[38] of Santa Barbara, California, decided that the method showed sufficient value to warrant a thorough trial. Because of the instability and the great variation in the toxicity of the colloid suspension of the metallic lead which greatly limited its clinical usefulness, Ullmann's main interest was to secure a more suitable lead preparation. Bischoff, Blatherwick and their coworkers[12,13] after several unsuccessful attempts with the metallic lead, suggested that lead orthophosphate, $Pb_3(PO_4)_2$, be used. This salt is stable in neutral solutions and therefore can be kept unaltered much longer. In the presence of only slight acidity it is changed to the acid phosphate, $Pb HPO_4$, which is a hundred times more soluble. The theory was advanced that because of this property and since malignant neoplasms contain a certain amount of lactic acid, the tumor cells would be affected as by the metallic preparation but without the severe general toxic injury to the patient.

In subsequent publications[39–41] Ullmann described in detail the immediate and late reactions observed following the administration of colloidal lead orthophosphate confirming beyond doubt that this substance is much less toxic to the organism than the colloidal metallic lead or its other salts. He also determined that the maximum benefit was obtained when the lead was combined with roentgen or radium therapy. An average dose of 80 milligrams of colloidal lead orthophosphate was given intravenously once a week, reaching a total of 400 milligrams and the irradiation was begun when from 200 to 300 milligrams had been injected. After four to six weeks the treatment was repeated until a total dose of from 500 to 600 milligrams was administered. If signs of lead poisoning appeared, 2 grams of calcium lactate in 1 quart of milk were given every twenty-four hours.

The introduction by Ullmann, and Bischoff and Blatherwick of the rather stable and decidedly less toxic colloidal lead orthophosphate has led to a number of clinical investigations. The majority of workers concentrated their attention on the use of lead as the sole therapeutic agent, chiefly in advanced cases of cancer which could not be treated by other means. It was repeatedly demonstrated that lead concentrates more readily in cancer tissue than in the surrounding normal tissue.[4,10,11,25,30,32,43] In a case of periosteal sarcoma studied by Bell[10] the tumor contained 12 parts per million of lead and the nearby normal bone only 1 part per million of lead. Osterberg and his associates[32] found the concentration of lead in the tumor greater than that in the normal tissue by four to five times. Nevertheless to produce notable clinical regression of the cancer it became invariably necessary to raise the dose of the colloidal lead administered to 400 milligrams or more. Several authors[3,4,5,19,32] insisted that the dose should be pressed to plumbism, with its symptoms of severe abdominal colic, pains in the arms and legs, anorexia, vomiting, loss of weight and more or less severe anemia. These symptoms were then combatted with various measures ordinarily used in chronic lead poisoning.[5,25] An acceleration of the elimination of the retained lead was also attempted by the administration of calcium mobilizing drugs and parathormone.

Other investigators used colloidal lead in conjunction with deep roentgen therapy or radium. Such a course was already

pursued by Stone and Craver[36] in 1927 by employing a suspension of metallic lead prepared by Woodard. Stone and Craver found that, if combined with irradiation, good improvements could be obtained with doses as small as 75 milligrams of colloidal lead given in a single dose. Their experience suggested that, especially in bone metastases from carcinoma of the breast, lead in conjunction with radium or roentgen therapy could cause regression sufficiently complete to account for greater palliation than was formerly possible. A similar situation was noted in advanced osteogenic sarcoma. A combination of intravenous colloidal lead orthophosphate and deep roentgen therapy was used in various types of cancer by Aub and Smithwick[3] and in a limited group of cases by Bargen, Horton and Osterberg,[4] and by others. Nearly always, the dose of the colloidal lead orthophosphate was increased to the point of intoxication.

An analysis of the final outcome in all these instances shows a rather disappointing picture. There is a unanimous opinion that colloidal lead alone, whether given in the metallic form or as orthophosphate, offers no cure for malignant neoplasms. When used in conjunction with surgery or radiation therapy in the advanced cases it seems to have some usefulness, but according to Bargen, Horton and Osterberg[4,32] lead intoxication is necessary to produce satisfactory results. On the other hand, Aub and Smithwick[3] believe that colloidal lead orthophosphate, even if given in very large doses and followed by deep roentgen therapy, is not only valueless but shortens the life expectancy by the severe symptoms of intoxication and the anemia it produces. Gould, Kullman and Shecket[19] who made a very detailed study of the effect of lead on the blood cells of cancer patients, likewise found that if progressive anemia once developed there was little likelihood of improvement after the lead treatment was stopped.

At Harper Hospital in Detroit colloidal lead orthophosphate obtained through the courtesy of Drs. Ullmann and Bischoff (and for the last few years supplied by the Crookes Laboratories of New York) has been used since 1928. The procedure employed, however, has been along somewhat different lines. Although in the beginning there was a tendency to use the method in all advanced cases of cancer, later, based on experimental investigations and clinical observations, its use was restricted to those instances in which the osseous skeleton was involved. The great majority of cases, by far, was represented by carcinoma of the breast with bone metastases. The present paper deals particularly with this group of cases.

It was already observed early that in chronic plumbism lead is stored mainly in the bone along with calcium phosphate in the form of lead orthophosphate,[2] or a similar highly insoluble salt. It thus seemed that the calcium and lead may have some similarity of metabolic behavior and that the deposition and mobilization of the two elements may also be similar. Furthermore, it appeared probable that the absorption and excretion of the colloidal lead injected for therapeutic purposes may be modified by the same agents that modify the absorption and excretion of the calcium, and in the same direction.[35]

Chemical analysis made by a number of investigators revealed that shortly after the intravenous injection of colloidal lead preparations, the largest amounts of lead were found in the spleen and liver, [13,17,20,21,24] and less frequently in the lungs.[38] The blood stream lost the lead rapidly[13,30,31] the excretion occurring mainly through the kidneys and all parts of the gastrointestinal tract. At this stage the osseous structures showed a relatively low concentration of the lead.

Throughout the first week, however, the lead deposited in the spleen, liver and lungs decreased rapidly[3] through excretion and through gradual migration to the skeleton (Fig. 1). Later the greatest part of the retained lead (from 39 to 100 per cent) was found in the bones and teeth, it being confined to the solid portion of the bone.

To further substantiate the affinity of the lead for the osseous system, a series of diffraction studies were carried out at Harper Hospital in rabbits. Doses of different amounts of colloidal lead orthophosphate were injected into rabbits and the animals killed at definite intervals. Various portions of the bone were then subjected to diffraction analysis and the results noted. It was found that the colloidal lead orthophosphate, which has a typical pattern, was deposited largely at the place of most active new cell growth where the metabolism was greatest, such as along the epiphyseal lines. It appeared that the lead did not enter directly into the permanent structure of the bone, but replaced the part normally played by the calcium in bone metabolism, for a limited time (Fig. 2). This interpretation finds additional support in the observations of Aub[1] who, in chronic lead poisoning, was able to increase the normal excretion of lead from two and a half to three times by the administration of mineral acids or ammonium chloride and sodium bicarbonate, and to nearly twice the normal by the administration of potassium iodide, thus proving that the calcium and lead metabolism are interrelated to a certain extent.

FIG. 1. Roentgenograms of the lower extremities of rabbits showing definite deposition of the lead along the epiphyseal lines.

Based on such considerations, it was assumed that the preliminary intravenous injection of colloidal lead orthophosphate would enhance the therapeutic efficacy of the roentgen therapy, especially in the malignant neoplasms with a more diffuse invasion of the osseous system. Three reasons were advanced for such an assumption. In the first place, as amply demonstrated above, the lead itself exercises a toxic action on the tumor cells; second, the roentgen rays produce a destructive effect in the well known manner; and third, the heavy lead ions deposited within the neoplastic tissue emit under the influence of the roentgen rays secondary electrons which add to the ionizing effect of the direct irradiation thus increasing to a certain extent the tumor dose. A good illustration of this latter effect is obtained by placing lead plates directly in contact with the patient's skin while administering supervoltage roentgen therapy as practiced, for example, in delineating the areas treated when the open field method is used. The secondary electrons emanating from the irradiated lead bombard the site of the closest contact of the lead plates with the skin. The reaction produced is superimposed on the skin erythema resulting from the direct action of the roentgen rays, with the consequence that a marked intensification of the redness is observed at the edges of the lead plates. This effect is not observed with deep roentgen therapy since apparently the range of the emitted secondary electrons is not long enough, but it is a very common occurrence

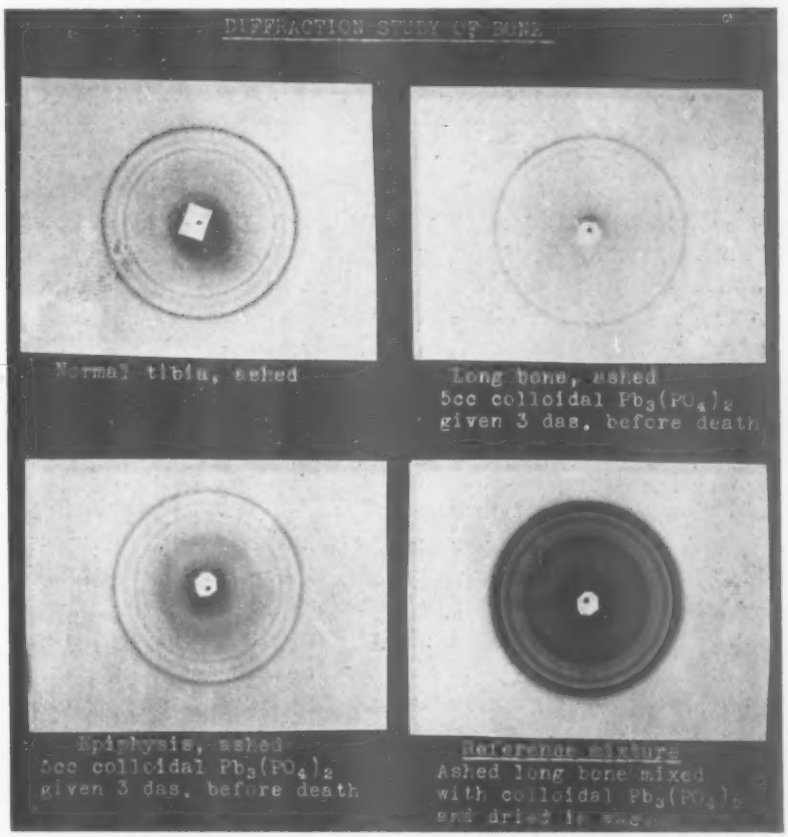

FIG. 2. It is demonstrated that that the colloidal $Pb_3(PO_4)_2$ is not deposited as such in the bone, but enters directly into the bone metabolism without destruction of the fundamental apatite structure. It probably replaces calcium or possibly magnesium in the structure.

with supervoltage roentgen therapy. Not infrequently the entire edge appears outlined, as if the erythema field were fenced in by a border of much deeper red (Fig. 3).*

The method employed has undergone, especially in the earlier days, several modifications. At first there was a tendency to give large total doses of lead producing a condition bordering on plumbism. However, since most of the patients were quite

FIG. 3. When protective lead plates are placed in direct contact with the skin while administering supervoltage roentgen therapy, the erythema field appears surrounded by a border of much deeper red, due to the added effect of the secondary electrons emanating from the lead.

ill to start with, the severe after-effects from the lead not infrequently added to rather than detracted from their discomfort. Similarly, a too intensive series of irradiation which was used in the beginning proved more of a disadvantage than an asset in the combination. The time interval between the injection of the lead and the starting of roentgen therapy had also to be carefully chosen. It was thought best to permit the greatest part of the circulating lead to be excreted and administer the irradiation during the deposition of the retained lead within the osseous system.

At the present time the procedure is more or less standardized. An average dose of 30 cc. of colloidal lead orthophosphate suspension containing 120 milligrams of lead is injected intravenously. Then three days later a series of deep roentgen therapy is given. As a rule, rays obtained with 200 kv., 1 mm. Cu, are used and full erythema doses are given per field in one seance. The number of fields selected for crossfiring depends on the physical measurements of the part of the body to be irradiated. Occasionally, in very heavy patients, supervoltage roentgen therapy is employed because of the greater depth dose. The entire series is completed in a period of from a few days to two weeks. A fractionation and protraction of the irradiation is rarely undertaken. Since not a few of the patients are quite ill and find it difficult to move about, hospitalization proves necessary in about 20–30 per cent of the cases. In the presence of pathologic fracture a suitable immobilization is provided for two to three months. The injection of the colloidal lead is repeated two months later and followed again within three to four days by a second series of deep roentgen therapy. The procedure is identical to that of the first series except for the fact that due to the marked improvement which has already occurred now only 10 per cent or less of the patients are hospitalized. This completes the course of treatment. Periodical check-up examinations are made thereafter at intervals of three months. When there is evidence that the carcinoma has spread to a new area, or that it has recurred, further lead, again in combination with irradiation, may be given at shorter or longer periods without fear of producing any general deleterious effect on the system. In one of the cases in our series a total of 1,200 milligrams of colloidal lead orthophosphate was injected

* While it has been shown many times (Quimby and Focht. Preliminary studies on dosage measurements with million volt roentgen rays. AM. J. ROENTGENOL. & RAD. THERAPY, 1941, *46*, 376–398) that this effect on the skin can be produced by almost any substance, the high atomic number of lead even in the weak concentration obtained makes it about eight times as efficient as a source of energetic photoelectrons as the average components of normal bone.

over a period of ten years, associated with twelve series of deep roentgen therapy with gradually reduced doses.

The administration of the colloidal lead in the amounts mentioned above carries practically no risk. The only contraindications are severe liver damage, nephritis and very marked anemia, with a hemoglobin below 30 per cent and a red corpuscle count below 2,000,000. In about 20 per cent of the cases the intravenous injection of the colloidal lead orthophosphate is followed within one to two hours by a chill and a temperature elevation up to 103° F. In another three to four hours the temperature drops to normal and no after-effects are observed. Occasionally, the chill and temperature elevation appear with a delay of twenty-four hours. Other complaints are slight nausea, anorexia and a feeling of tiredness. All of these symptoms, however, as so mild that the injection is nearly always given with the patient ambulatory and even the very ill patients are hospitalized only for the duration of the roentgen therapy series.

The complaints in conjunction with the invasion of the osseous skeleton by the malignant neoplasms begin to abate in about ten to fourteen days. In the great majority of the cases the pain, unless there is a pathologic fracture or a very wide dissemination, completely disappears within six to eight weeks. In three months there is a very solid reossification of the formerly destroyed areas of the bone permitting the resumption of limited activities. This alleviation of the distressing symptoms is the more remarkable since in an otherwise hopeless situation the efficacy and usefulness of most patients is greatly increased for the remainder of their expected life. Periodical roentgenograms show that the affected bone is often rendered so dense by the lead and roentgen therapy that it appears more compact than the normal bone

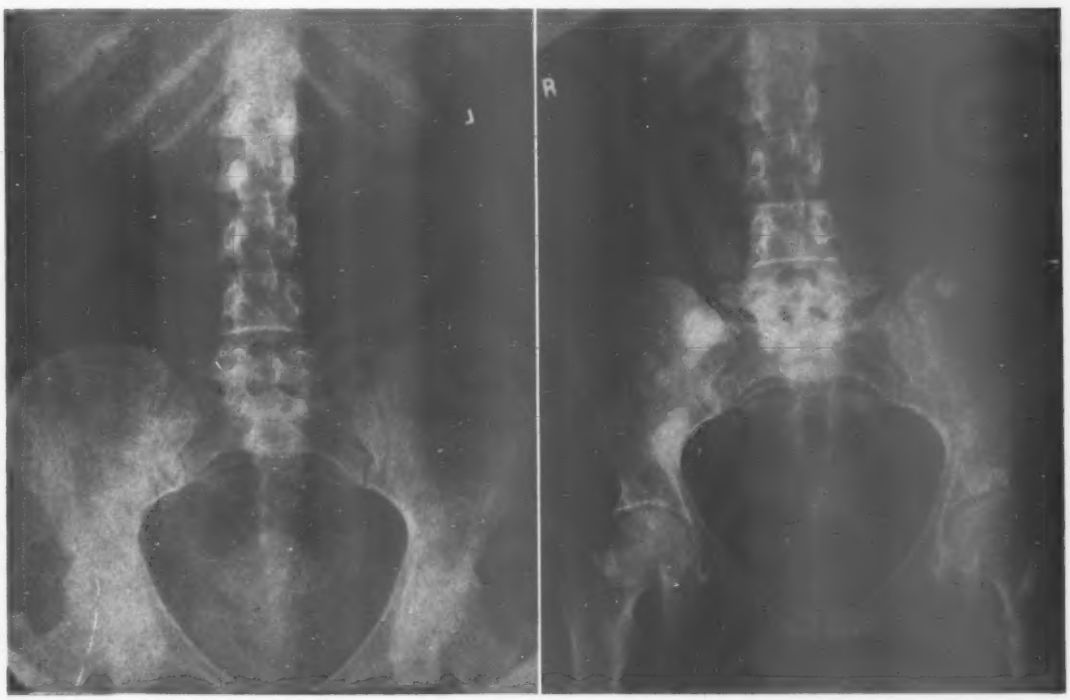

Fig. 4. *Left:* questionable areas of osseous rarefaction due to metastases from a primary carcinoma of the breast. *Right:* same, six months later, after two series of intravenous injection of colloidal $Pb_3 (PO_4)_2$ associated with deep roentgen therapy, showing markedly increased opacities replacing the formerly destroyed areas.

(Fig. 5 and 10). At times, when at the initial examination there were questionable areas of rarefaction, following the completion of the treatment well demarcated dense nodes are visualized on the roentgenograms (Fig. 4), leaving no doubt about the correctness of the diagnosis.

A compilation of the final results shows that during the past twenty years 2,406 cases of carcinoma of the breast have been treated at Harper Hospital and that, of these, 355 have received a combination of intravenous colloidal lead orthophosphate and deep roentgen therapy following the development of bone metastases. It may be said that the symptomatic improvement in 95 per cent of the cases was very satisfactory. The average survival from the time of the institution of the treatment, however, amounted to only three years, the cancer in the interim having continued to extend to other regions and viscera until it became generalized. In 4 per cent the survival has been more than five years (Fig. 6, 7 and 11), the longest case in our records having lived ten years (Fig. 8, 9 and 12). There have been no permanent cures.

More recently, attempts were made to use some form of a radioactive colloidal lead orthophosphate for the intravenous injections, in the hope that the substance deposited in the osseous system might continue to act as a source of local radioactivity after the roentgen therapy series had been concluded. This would add to the three effects already mentioned a fourth effect, that of a prolonged internal radiation, the duration of which would depend on the half-life of the particular radioactive isotope inserted in the preparation and on the rate of excretion of the lead from the osseous system.

In a preliminary series of experiments "tracer" studies were made by using col-

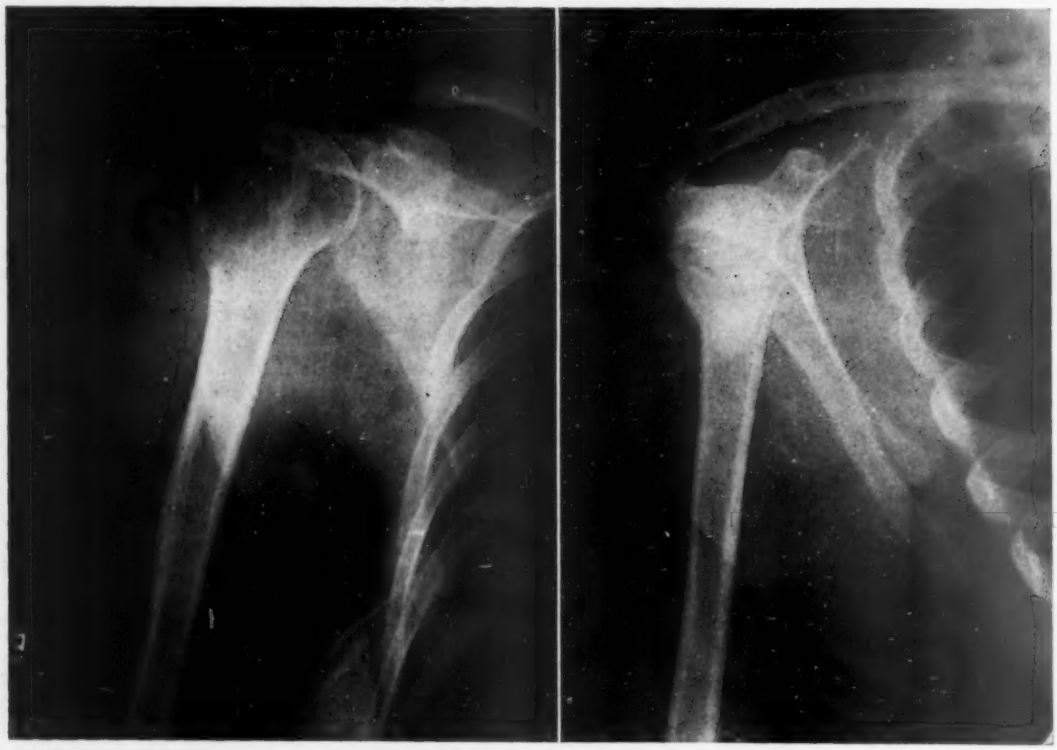

FIG. 5. *Left:* metastasis to the head of the humerus from a primary carcinoma of the breast. *Right:* same three years later, after two series of colloidal $Pb_3(PO_4)_2$ and deep roentgen therapy. Patient died after four years.

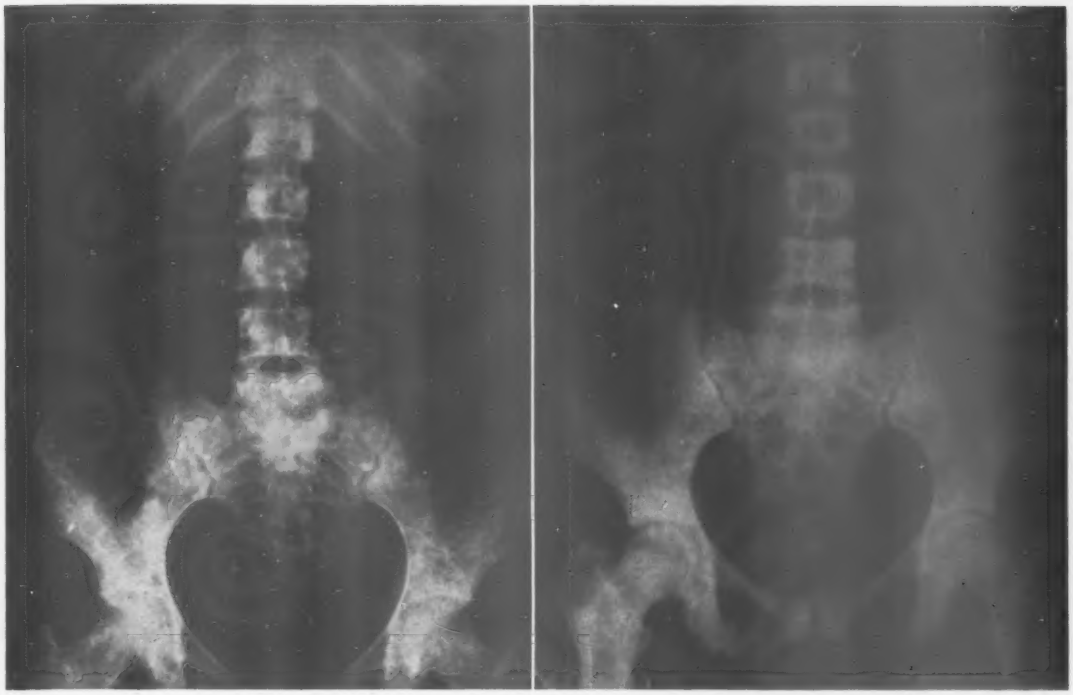

FIG. 6. *Left:* very extensive metastases to the entire osseous skeleton, from a primary carcinoma of undetermined origin. *Right:* same, six years later, after several series of colloidal $Pb_3(PO_4)_2$ and deep roentgen therapy showing remarkable bone regeneration. Patient died after eight years with general visceral metastases.

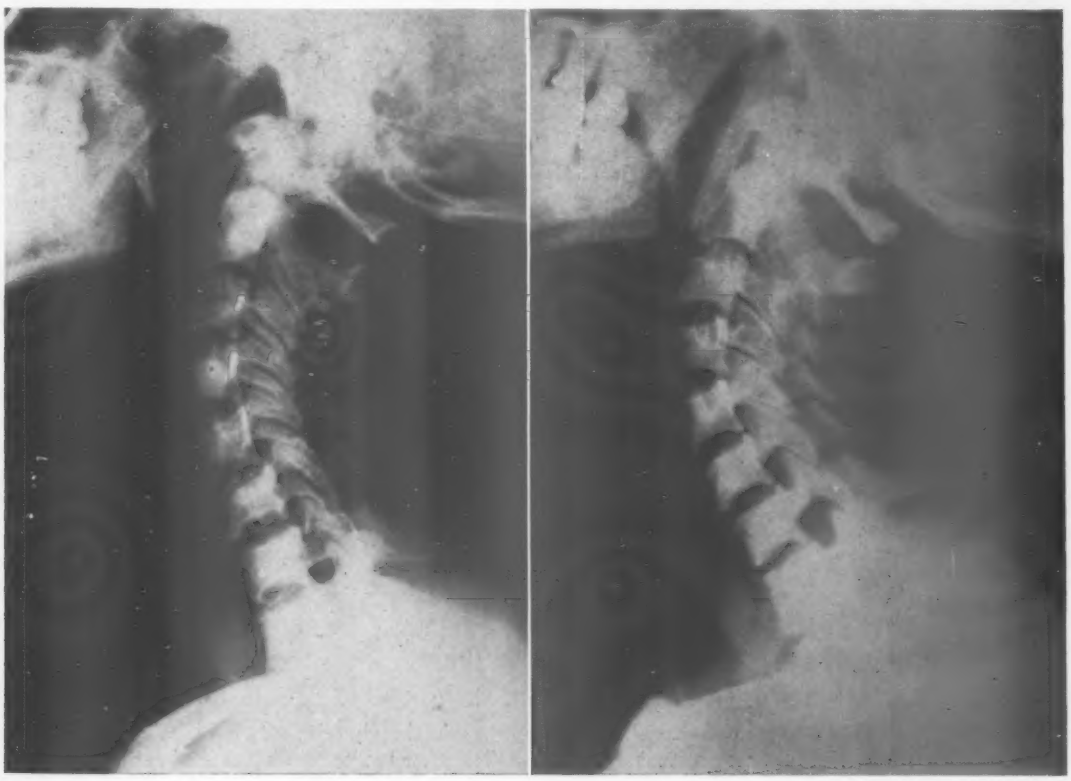

FIG. 7. Same case as in Figure 6, showing metastatic involvement of the cervical spine. *Left:* before treatment; *right:* six years after treatment.

FIG. 8. *Left:* extensive nodular metastases to the pleura with massive effusion following a primary carcinoma of the breast. *Right:* same, nine years later, showing complete fibrosis of the affected hemithorax as a result of three series of colloidal $Pb_3(PO_4)_2$ and deep roentgen therapy.

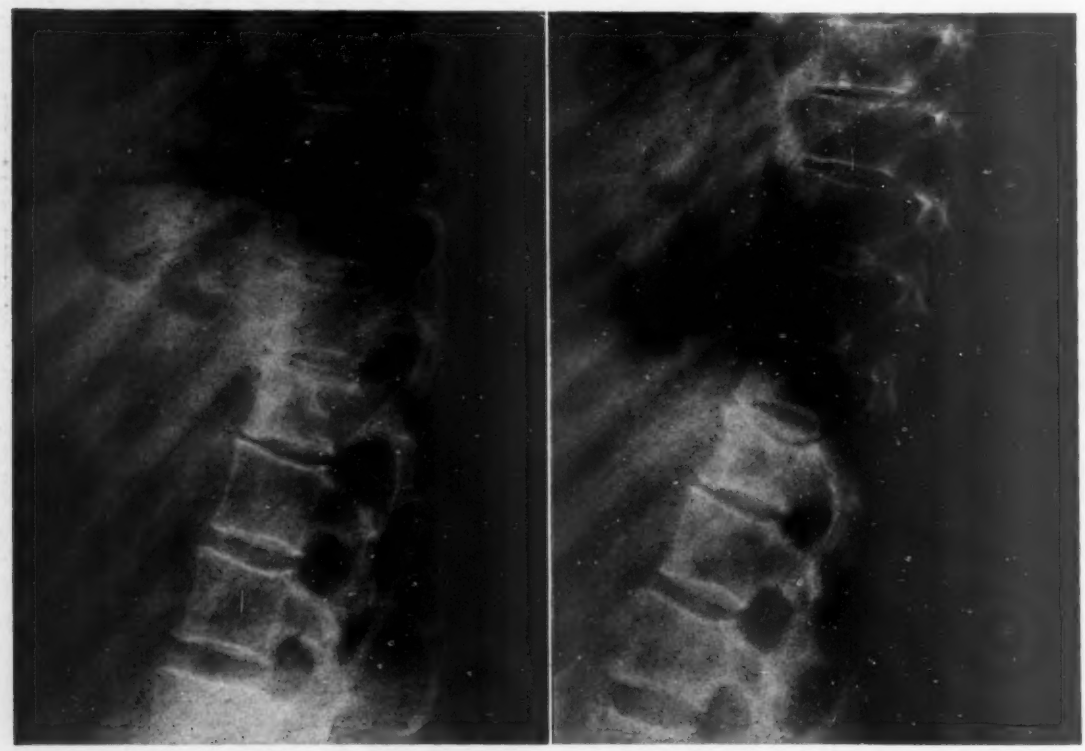

FIG. 9. Same case as in Figure 8. *Left:* seven years after the original treatment metastasis developed to the body of the twelfth dorsal vertebra. *Right:* following two additional series of colloidal $Pb_3(PO_4)_2$ and deep roentgen therapy good reossification occurred. Patient died after ten years with extension of the carcinoma to the brain.

loidal lead orthophosphate containing radioactive phosphorus. This material was prepared by Dr. Henrietta Hayden according to the following modification of the standard procedure:

Use 4.5 grams of gelatin dissolved in cold water, bring to boiling and add 1.25 grams of lead chloride. Then dissolve 1.3 grams of sodium phosphate (Na_3PO_4) in water. Add the required amount of radioactive phosphorus to give 0.1 millicurie of the phosphorus per 30 cc. of final solution, adding that to the lead chloride and gelatin which has previously been mixed. Then, while warm, add the sodium phosphate slowly. Dilute to a total volume of 250 cc. The entire procedure is done under sterile conditions. The solution is bottled, in this instance 30 cc. in each individual bottle. This is sterilized for one hour a day at 90° C. for four successive days.

The material so obtained was then injected into 7 three month old rabbits intravenously in varying amounts. The animals were followed closely for toxic manifestations, of which there were none, even though the dosage in some cases was five times that ordinarily administered to patients. The rabbits were sacrificed at intervals of nineteen, thirty-five, fifty-five, and sixty-eight days. Specimens were taken from the kidneys, liver, spleen, brain and epiphyseal areas and carefully studied for radioactivity. It was found that nineteen days following injection 8.78 per cent of the lead orthophosphate was in the liver, 1.54 per cent in the spleen and 0.05 per cent in the kidneys. At the end of thirty-five days 5.55 per cent was in the liver, 0.28 per cent in the spleen and no significant amount in the kidneys. After fifty-five days 0.05 per cent was found in the liver. Radioactivity remained present after sixty-eight days, but was insufficient for careful measurement. A count with the Geiger-Müller counter was considered significant only if it was at least twice the background.

From these findings it was concluded that the liver gives up its lead phosphate slowly compared to the spleen, which, however, contains a greater percentage for its volume (average weight of spleen being 2 grams and of liver 100 grams) in the first three weeks or more. The kidneys have little lead phosphate at any time after nineteen days. It was felt that inasmuch as no significant counts were obtained from the brain at any time, little free phosphate ion was present.

FIG. 10. *Upper:* massive destruction of the body of the ilium by metastasis from carcinoma of the breast. *Lower:* same, seven years later, after three series of colloidal $Pb_3(PO_4)_2$ and deep roentgen therapy, showing very compact reossification. The patient is alive after eight years.

Roentgenograms made at regular intervals of the extremities of the animals indicated, as did the autopsy specimens, an increasing deposition of the lead phosphate

FIG. 11. *Left:* massive destruction with complete collapse of the body of the fifth lumbar vertebra from a malignancy of unknown origin. *Right:* same seven years later, after several series of $Pb_3(PO_4)_2$ and deep roentgen therapy. There is a good support of the collapsed vertebra and the patient is at the present time symptom-free.

FIG. 12. *Left:* metastatic lymphosarcoma of the upper tibia (proved by biopsy). *Right:* same five years later, showing complete regeneration of the bone. The patient is in excellent condition ten years after the onset of the lymphosarcoma, during which interval she received fifteen shorter or longer series of deep roentgen therapy and three injections of colloidal $Pb_3(PO_4)_2$ (for the bone metastasis).

in the epiphysis. These findings agree with those of Kehoe and Thamann[23] who found that the lead phosphate compounds are relatively inert and are excreted slowly but steadily. They, too, found that the lead was retained for a longer period in the liver than the spleen with eventual loss to the skeleton and excretion.

Following these preliminary experiments a preparation containing 100 microcuries of radioactive phosphorus (P^{32}) and 120 mg. of lead per 30 cc. of solution was made and injected intravenously into 6 patients, each of whom had neoplastic involvement of the bones. The primary lesions were represented by chordoma, carcinoma of the

prostate, carcinoma of the sigmoid, and carcinoma of the breast. Careful studies were carried out with the aid of the Geiger-Müller counter to determine the localization of the "tagged" phosphorus. Although in some of the patients the measurements were extended over a period of more than two weeks, no significant localization to the known tumor sites could be ascertained. This was rather surprising but it is possible that with a greater concentration of the "tagged" phosphorus or by "tagging" the lead rather than the phosphorus different results may be obtained. Obviously further exhaustive investigations are necessary.

SUMMARY

A detailed review of the literature shows that the colloidal lead orthophosphate, $Pb_3(PO_4)_2$, introduced by Ullmann and Bischoff, is considerably more stable and less toxic than the electric suspension of metallic lead used by Bell for the treatment of cancer.

Diffraction studies performed in rabbits at Harper Hospital confirmed the affinity of the lead for the osseous system, the largest deposition occurring along the epiphyseal lines and at the place of most active new cell growth. Apparently, the lead replaces for a limited time the part that calcium normally plays in bone metabolism.

The preliminary intravenous injection of colloidal lead orthophosphate in conjunction with roentgen therapy leads to a threefold effect in the malignant neoplastic invasion of the osseous system: (1) the lead has a certain toxic action in itself; (2) there is a direct destructive effect of the roentgen rays; and (3) the heavy lead atoms deposited within the tumor area emit, under the influence of the roentgen irradiation, ionizing secondary electrons which also act on the carcinoma cells.

The method has been used during the past twenty years in a series of 355 cases of bone metastases chiefly from carcinoma of the breast. In 95 per cent of the cases the immediate palliative effect was remarkable. The average survival amounted to three years. In 4 per cent the survival was more than five years. The case which survived longest lived ten years, but there were no permanent cures.

More recently attempts were made to use radioactive lead orthophosphate to add internal irradiation, if possible, to the above enumerated three-fold effect. In a series of preliminary experiments tracer studies were carried out in rabbits and some patients by injecting a specially prepared colloidal solution of the lead orthophosphate in which the phosphorus was "tagged." The results, in the main, substantiated the findings arrived at by chemical and roentgen diffraction analysis. However, further investigations, especially with "tagged" lead, are necessary, before worth while therapeutic efforts can be undertaken.

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THE SIMULTANEOUS DISAPPEARANCE OF TREATED AND UNTREATED TUMORS AFTER IRRADIATION

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IN SOME of our cases of multiple tumors, the treatment of one lesion was followed by the simultaneous disappearance of others. This has happened frequently enough to make the discussion of this topic of interest. Occasionally a tumor may disappear without treatment. The human body can, through some physical or chemical change, occasionally cause the disappearance of tumors. Radiation treatment of one lesion starts this natural process or enhances it. The local irradiation effects carried by the blood and lymph stream to the untreated areas may cause them to disappear. This disappearance of untreated lesions, along with treated ones, can occur in benign conditions of the skin such as psoriasis, hemangiomas, and warts. Occasionally the metastases of malignant tumors disappear with the irradiation of the primary lesion.

In some of our cases of myelogenous and lymphatic leukemia, lymphosarcoma and Hodgkin's disease, the irradiation of the spleen, or one particular group of glands causes the distal involved glands to disappear. At times in Hodgkin's disease, the fever, the skin eruption and itch disappear in twenty-four to forty-eight hours after the local treatment of the spleen.

Recently a patient in whom a malignant melanoma had been incompletely removed from her lower leg was sent to our clinic for irradiation. On admission she had extensive metastases to the groin and hundreds of little implants along the entire extremity. Roentgen therapy was given to the groin more as a gesture than anything else for these lesions are extremely radioresistant. About eight weeks later, it was a great surprise to see that not only had the groin metastases disappeared but also the leg metastases.

Irradiation may stimulate the natural reparative processes, and in some cases this is enough for a cure. The cure of some malignant tumors after an attack of erysipelas, relapsing fever, or by the administration of Coley's toxin, may be helping nature in a similar way.

One of our patients with proved Hodgkin's disease had complete disappearance of enlarged axillary and inguinal glands and a large mass in the epigastrium after a reaction as the result of a transfusion. Peculiarly he did not have a temperature reaction but rather a severe eczema involving both the skin and mucous membrane. We had had reactions from transfusions for several weeks at this time, the reactions starting when a batch of transfusion bottles came in containing sodium citrate 1.33 grams; dextrose C. P. anyhdrous 3 grams; citric acid U. S. P. 0.47 gram per 100 cc. There was 130 cc. of this solution in each bottle. These reactions had never occurred when we used our regular formula and they promptly disappeared when we changed over to it again. In this regular formula each 100 cc. of solution in the transfusion bottle contained dextrose C. P. anyhdrous 3.1 grams; sodium citrate U. S. P. XII 1.37 grams. There was 140 cc. of such solution in each bottle.

Was the citric acid the cause of the transfusion reaction? It was the reaction that caused the Hodgkin's lesions to disappear, and not the citric acid itself. The body manufactured some substance during the reaction which was injurious to the Hodgkin's granuloma. Possibly rapidly growing tissues cannot stand such sudden, shocking, destructive reactions as can normal tissues.

There are reported in the literature at least four hundred hopeless cases of malignant new growths in which cures resulted

after such inadequate procedures as a biopsy, an incomplete operation, after some secondary infection, or some unexplained fever.

Sussman[4] mentions the disappearance of lung metastases in 3 patients after the removal of only the primary lesion. One was operated on for a suprarenal tumor and is alive twelve years after the operation, one had a Wilms' tumor removed and is alive two years after the operation, and the last one was operated on for a hypernephroma and is alive three years after the operation.

All of us have seen cases in which metastases have remained the same size for years, the patient finally dying of some other disesae. Recently a patient died of heart disease in whom a breast amputation was done fifteen years before for a rapidly growing tumor. At death no recurrence was found about the breast scar but hundreds of metastases imbedded in fibrous tissue and calcification were found in the pleura and adjacent parts of the lung. Here nature was able to retard metastatic growth and imbed the tumor tissue in connective tissue and cartilage.

The human body is constantly making substances to combat tumor cell growth. When only a few tumor cells invade the blood stream from a primary growth, these cells are quickly destroyed. They never have a chance to gain a new foothold. It has been observed that in experimental animals a tumor embolism must contain at least 50,000 cells in order for a metastasis to gain a foothold and survive. The natural reparative processes of the body can destroy a few hundred metastatic cells but not many thousands. Some organs of the body can handle them better than others. The internal secreting glands such as the thyroid, pancreas, and so forth, destroy them easier than the lung and metastases rarely occur in these organs.

In the urine of some experimental animals, in which new growths were being produced by carcinogenic substances, there was found a non-carcinogenic hydroxide product of the carcinogenic substance being used to produce the tumors.

In some cases the rate of tumor growth, and tumor destruction by the normal tissues remain the same. In our clinic a boy of about nineteen years of age has a proved osteogenic sarcoma of the rib which has remained the same size for at least ten years. At operation it was found that it would be impossible to remove the growth and nothing but a biopsy was done.

At times the explanation of distal reaction to local treatment is adequate, as in the cases of disappearance of metastases of breast carcinoma with the irradiation of actively functioning ovaries. Since ovarian secretion stimulates the growth of mammary glandular tissue, the removal of this stimulation deprives the metastases of their growth activity. The administration of testosterone in some cases causes the disappearance of metastatic breast carcinoma by depressing this ovarian activity. Since uterine fibroids are known to be due to hypersecretion of estrin, one can see how the decrease of this secretion by irradiation of the ovaries can stop the growth of this tumor. Also since a hypersecretion of the male gonad increases the growth of the prostate, it can be seen how methods of reducing this secretion can be of benefit in prostatic cancer and its metastases. There also seems to be some foundation for understanding the decrease of organic activity by the irradiation of the corresponding neural segment along the spinal cord. By so doing alterations in the nervous and arterial functions occur in these organs.[1]

A study of what local chemical and physical changes occur with irradiation and how many of these changes can be transmitted by the blood and lymph stream would be of value. The subject, however, is not so simple. In a cancer patient there are numerous blood and lymph changes. Some of these blood and lymph changes are secondary to the cancer growth, some may be primary and the cause of the

growth. Many of these changes may be nature's method of combatting the new growth.

A brief review of these various chemical and physical changes will be of value and possibly shed some light on how the body cures new growths and whether irradiation works in the same or a different way.

At first let us review briefly how a new growth differs from a normal one and how the new growth affects the blood stream and body fluids.

In a new growth there are microscopic, physical, colloidal, chemical, enzyme, protein, carbohydrate, and lipoid changes from normal.

The microscopic changes are well known. The tumor cells show features of anaplasia, loss of specific form and polarity, variation in size, multiform nuclei, atypical mitosis, and especially an increase in chromatin content of the nucleus. This increase in chromatin signifies an increased nutrition and increased powers of growth. There is an increase in the size of the nucleolus and there are changes in the number and sizes of the chromosomes.

The permeability of the cancer cell membrane is increased, and an increase in the water content of the cell occurs. Usually the more active the tumor, the greater the amount of water.

In malignant tumors there is a relative increase of potassium over calcium whereas in benign tumors the opposite is true. The inorganic salts of a cancer cell are decreased.

The extracts of cancer tissue have greater reducing powers than normal and this expresses itself in the blood serum, for the blood serum of cancer patients reduces methylene blue to a leuko base while the normal blood serum does not.

There is a change in the total protein and nitrogen contant of the new growth. While the total protein and nitrogen is less than normal certain fractions are greater. The globulin portion of the protein is relatively increased over the albumin. The globulin is 82 per cent of the total proteins instead of the normal 30 per cent. There is an increase in fibrinogen. The incoagulable proteins such as histones and protamines are increased. The amino acids necessary for life, such as lysin, cystine, and tryptophan are increased. These increased protein changes in the cancer cell manifest themselves in the blood and body fluids, and many tests have been developed for this increase, such as the Suranyi test, the anaphylaxis test, Botelho's test in which precipitation of globulin occurs with weak acids, and the photochemical test, in which precipitation of histones, protamines, and globulins occur with silver nitrate. The coagulation time is decreased.

Carbohydrate changes occur in a cancer cell. Cancer cells can burn sugar aerobically and anaerobically to lactic acid only. Normal cells can burn sugar down to carbohydrate and water. The cancer cell therefore is more acid than the normal one, and affects the blood this way also. The neutral red test has been developed to show this change.

The lipoid changes in a cancer cell are the most important. There is an increase in both cholesterol and lecithin, and this increase manifests itself in both the blood and the lymph stream. A great number of blood cancer tests probably is based upon the fact that the presence of increased cholesterol lowers the surface tension and causes flocculation and precipitation. The following tests are based upon this characteristic: miostagmin test, Shaw-Mackenzie test, Wiel-Braun test, Bozzo-Lombardi test, Kahn test, Freund-Kaminer test, Fry's flocculation test and eosin test.

It is probably also this increase in cholesterol which accounts for the increase in the water content of the cancer cell and its increase in permeability.

The enzyme contents of a cancer cell are changed. There is an increase in the protein digestive enzyme ereptase. The carbohydrate enzyme glutathione is present in greater amounts. The lipases present digest all fats with the exception of cholesterol.

This fact is worth remembering.

In a cancer patient these changes, caused by the growth and carried by the blood and lymph stream throughout the body, affect the normal physiological processes of other organs. In some, they increase the functions, in others they diminish them. They cause an increase in the size of the pituitary and the adrenal cortex. They cause a hypertrophy of the entire reticulo-endothelial system. The liver, the gastro-intestinal tract, the muscular and skeletal and hemopoietic system are depressed. This in part explains the loss of weight, anemia, cachexia, and debility in many cancer patients.

How many of these cancer cell and blood changes are primary, and how many are secondary to the growth, are not definitely known, but I believe that of all the changes, the cholesterol changes are the most closely associated with the cause of cancer, rather than secondary to it, for the following reasons:

Cholesterol, when heated, will cause tumors in rabbits and mice. Cholesterol is closely related chemically to the coal-tar carcinogenic substances, which have produced in lower animals practically all the malignant growths known to man. It is closely related to male and female sex hormones, which under certain conditions have produced cancer, and also to ergosterol and vitamin D, which under actinic stimulation might be responsible for carcinoma of the skin.

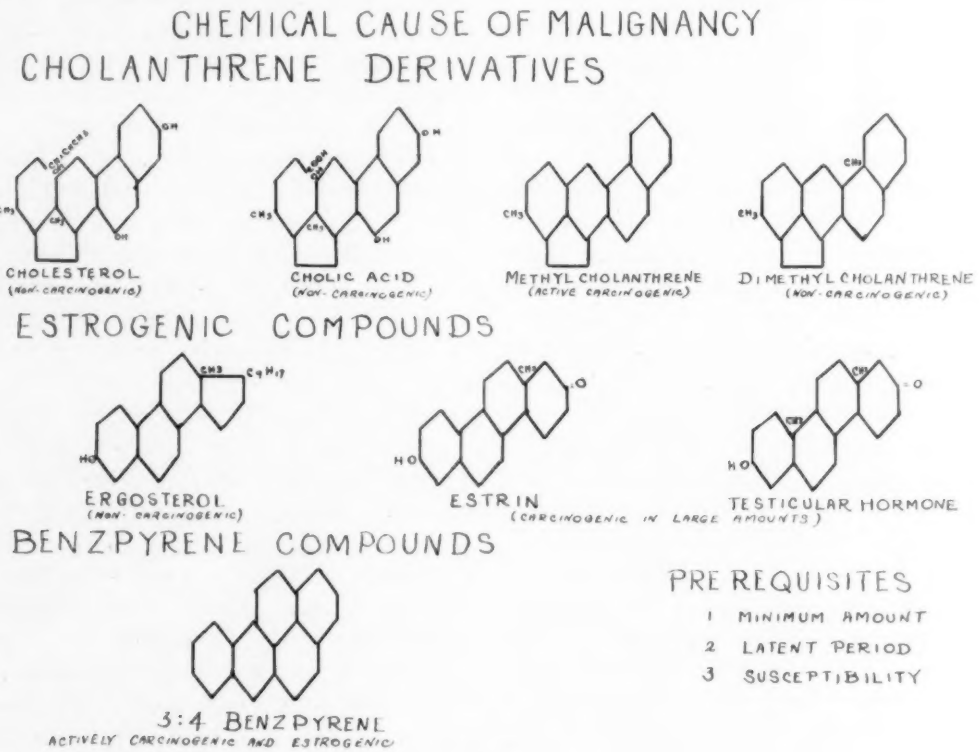

FIG. 1

In Figure 1 is shown the close chemical relation of cholesterol, ergosterol, and the gonadal hormones, to the carcinogenic substances. In the production of experimental new growths in lower animals certain prerequisites are necessary: The carcinogenic substance used must be of sufficient amount; the time over which it is used must be long enough; and the animals in which it is used must be susceptible to it.

By certain chemical changes cholesterol, which is present in every cell of the body,

could be converted to carcinogenic substances. Irritation, inflammations, ulcerations, and so forth, over a long enough period in a patient whose tissues are susceptible, might cause this carcinogenic transformation of cholesterol. Mild cholesterol changes might cause hyperplasia and proliferation of cells, and greater cholesterol changes might produce the disorganization which occurs in carcinoma.

Also note how the addition of a CH_3 to the actively carcinogenic substance, methyl cholanthrene renders it non-carcinogenic (dimethyl cholanthrene). It is possible that in some similar way the body occasionally cures its own new growths. Possibly the future cure of carcinoma awaits some similar simple chemical change.

Irradiation also causes local changes, and these changes manifest themselves distally by means of the blood and lymph stream. The local changes seen microscopically are an increase in the size of the cells and their nuclei. The greater the irradiation, the greater the swelling. The more abundant the circulation in the neighborhood of the new growth, the greater the extent of this cellular swelling. The cells swell because irradiation increases the cell permeability and the osmotic pressure within the cells, thus water enters the cell and the nucleus. The permeability of the cell membrane is unidirectional. Water can go in but waste products of metabolism cannot get out, unless the cell dies and breaks up.

The irradiation causes physical and chemical changes in the cell by means of ionization. The atoms of the cell absorb a quantum of radiation and lose electrons in the form of corpuscular rays. The ionization thus produced modifies the electrical charge of the colloids and crystalloids in the cells and tissue fluids.

The colloids in the cells have negative and positive charges of electricity. They are important in the function of protoplasm, because of their ability to alter surface tension, absorption, and catalytic properties. The consistency of protoplasm, whether fluid or gelatinous, the quantity of water imbibed, depends upon the colloids. Many of the larger molecules and loidal particles are broken into smaller ones by ionization, thus increasing the osmotic pressure.

The properties of colloids are greatly influenced by physical, electrical and chemical conditions of the medium in which the colloid is suspended. The medium in which protein and lipoid colloids function is a saline one. Ions of these saline or crystalloid molecules, in the metabolism of cells, pass in and out of cells, and by these ions the alkalinity of the cell is maintained, oxygen and food are brought to the cell, carbon dioxide and waste materials are removed. Electrical changes that occur in muscle, nerve tissue, etc., also depend upon the ionic action of crystalloid substances. As a result of ionization caused by irradiation, the normal electrical charges of these saline ions are changed, and this along with the altered colloids disturbs the functions of the cell, its metabolism, and life.

Many colloids and crystalloids have no electrical charge, and need none for proper function. The ionization of these produces improper metabolism, and the change may be sufficient to injure or destroy the cells.

The chemical changes which follow ionization are many. Changes occur in the minerals, the proteins, the carbohydrates, the lipoids and, the enzymes of the cells. Oxygen can be converted into ozone, metals are oxidized, some salts are decomposed, and a change occurs in manganese. Oxyhemoglobin is often changed into methemoglobin. There is an increase in the coagulation of globulin. Organic matter decomposes, fatty tissue becomes harder, and cholesterol and its salts are made to disappear from solution. This seems especially important in view of the fact that the principal cause of cancer may be due to activated products of cholesterol. The various cell enzymes such as trypsin, pepsin, and invertase, are inactivated by irradiation, and sucrose may be inverted.

These changes caused by ionization in the cells, the tissue fluids and the intracel-

lular medium are probably carried by the blood and lymph to all parts of the body. That irradiation produces a distal effect is well known. These patients complain of dizziness, weakness, sleepiness, loss of appetite, nausea and vomiting. Radiation sickness is probably due in part to the physical and chemical changes of ionization and in part to the products of disintegration of sensitive cells which are circulated throughout the body by the blood and lymph stream. Some say that the blood of patients treated with radiation contains a substance which is toxic to plant test objects and that this is the cause of radiation reactions. Others believe that it is due to a decrease in the amount of blood cholesterol as a result of ionization and that this decrease in cholesterol causes radiation sickness through irritation of the vagus. Some claim that radiation sickness is due to a decrease in blood sugar and vitamin B_1. Giving these patients increased sugar, liver extracts, and vitamin B_1 does improve their radiation sickness. Upon the basis that local ionization produces a damaging effect to the entire reticulo-endothelial system, congo red has been given to prevent this radiation damage. Lofstrom and Nurnberger[3] think that radiation reaction is due to histamine-like substances. These substances have been found in fresh blood samples after irradiation. They give benadryl in 50 mg. doses three to four times a day for several days, with good results.

At any rate, whatever be the cause of radiation sickness, there are definite distal reactions to local irradiation. The local physical and chemical changes due to irradiation affect the blood stream and then the distal lesions. When these distal lesions are radiosensitive, they are deleteriously affected. It is most often the radiosensitive lesions, such as the lymphosarcomas, the leukemias, Hodgkin's disease, hemangiomas and warts which are affected.

To determine which specific change produces the disappearance of distal lesions will require a great deal of research. In a great many ways the finger points toward some change in both the amount and the chemical character of cholesterol. As has already been shown, a slightly chemical changed cholesterol seems responsible for new growths. Cholesterol is increased in the cancer cell. Cholesterol is closely allied chemically to carcinogenic substances. Irradiation causes cholesterol to disappear from solution. It causes blood cholesterol to fall. There may be a change in the growth stimulating character of cholesterol as well as in the amount, and this probably is not determined by the usual method of cholesterol analysis. This change in cholesterol both locally and in the blood stream may deprive the primary lesion and its metastases of their growth stimulating element and in this way cause their disappearance. These cholesterol changes may be produced by causes other than irradiation. The low cholesterol level in starvation has caused certain experimental tumors to disappear. New growths will occasionally disappear without irradiation or any other form of treatment. In these cases, the body may not only lower the blood cholesterol, but also change it chemically so that it is not growth stimulating.

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THE DIAGNOSIS OF SUPRASELLAR TUMORS BY PNEUMOENCEPHALOGRAPHY*

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THE localization of intracranial tumors has always constituted a fascinating problem from the standpoint of neurological diagnosis. Great advances have been made in this regard as a result of a more accurate determination of the diagnostic significance of symptoms and signs with reference to cerebral localization. Nevertheless there still often remains the problem of accurately establishing the nature of the lesion even though the localization is made evident by the symptoms and signs. The suprasellar region has long been an area in which the conclusive establishment or exclusion of a tumor was associated with uncertainty and frequent errors in diagnosis. The fact has been recognized that relatively large neoplasms could exist in the suprasellar region without producing definite localizing clinical manifestations at a time when neurosurgical intervention would be most beneficial to the patient.

Efforts to cope with the diagnostic problem presented by a suprasellar expanding lesion have been made and have contributed to a partial solution of this problem. Foster Kennedy[5] called attention to the syndrome bearing his name in 1911. At that time he considered it to be "an exact diagnostic sign" of tumors or abscesses in the subfrontal region, but he later broadened the concept of this syndrome to include aneurysms[6] in the same region. The syndrome as originally described consists of the presence of a central scotoma and primary optic atrophy an the side of the lesion with papilledema on the opposite side. When present, this syndrome has been diagnostically valuable but it does not occur in more than a relatively small percentage of tumors situated in the suprasellar region. Even when it does occur, a recent report by Yaskin and Schlezinger[13] has shown that the syndrome cannot be considered as pathognomonic of neoplasms but may be a result of arteriosclerotic compression of the optic nerves.

Another contribution to the early diagnosis of tumors in the suprasellar region has been the emphasis placed upon the visual field defects which may occur in such cases. Most helpful in this regard is the characteristic bitemporal hemianopic visual field defect but this is by no means a constant manifestation. Not uncommonly the visual field defects are of a bizarre form in which both central and peripheral defects of an expanding sector type are observed. These have been described as constituting a prechiasmal syndrome and the significance of scotomatous field defects in the diagnosis of suprasellar meningiomas has been emphasized recently by Schlezinger, Alpers and Weiss.[10] Similarly, defects in the fields of vision in cases of suprasellar hypophyseal duct neoplasms have been investigated by Wagener and Love.[12] Although such visual field defects are an important consideration in the early diagnosis of suprasellar tumors and are present sooner or later in nearly all such cases, it must be realized that these visual field defects are not conclusive evidence of an expanding lesion but may also occur in such conditions as optochiasmatic arachnoiditis, multiple sclerosis, syphilitic optic atrophy, and encephalitis. The differential diagnosis has been difficult and neurosurgical intervention has often been delayed until such time as the patient's vision is irreparably damaged or a tumor has assumed such dimensions that its removal constitutes a threat to survival.

Several observers have explored the pos-

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sibility of contrast visualization with iodized oil as a means of detecting tumors in the suprasellar region. Balado and Pardal[2] described a method utilizing iodoventriculography, and reported filling defects in the floor of the third ventricle. Subsequently, Carrillo[3] reported his results using a similar diagnostic procedure. Schüller[11] suggested the use of concentrated lipiodol for the purpose of cisternography. Since the use of iodized oil intracranially is hazardous, it is questionable whether these methods are deserving of routine clinical use.

FIG. 1. Case 1, S. G. (J. H. No. GH1861), female, aged thirty-six. History of sudden awareness of complete amaurosis on the left followed over a period of eighteen months by frequent generalized headaches. Neuro-ophthalmologic examination disclosed pallor of both optic discs; amaurosis of the left eye and temporal hemianopia of the right eye. Laboratory data, including a spinal fluid examination, within normal limits. Roentgenogram of skull negative. Pneumoencephalogram normal except almost complete obliteration of the cisterna chiasmatis. Diagnosis: suprasellar meningioma, verified.

Dyke and Davidoff[4] were the first to recognize the value of pneumoencephalography in the diagnosis of suprasellar tumors and they described the filling defects in the cisternae surrounding the optic chiasm. More recently Balado and Oribe[1] have reported similar cases investigated by means of pneumoencephalography in which visualization of the chiasmatic cistern and the floor of the third ventricle was said to have been improved by roentgenography with the head upside down.

In an attempt to determine whether a conclusive diagnosis of a tumor in the suprasellar region could be made early by means of routine pneumoencephalography, it was decided to review the pneumoencephalograms which were done in 5 patients who had a diagnosis of suprasellar neoplasm. This survey disclosed a striking alteration in the appearance of the cisterna chiasmatis, best described as obliteration,

FIG. 2. Case II. B. D. (J. H. No. GH7059), female, aged sixteen. History of headaches for three years with periods of remission; vertigo for three months; impaired memory and blurring of vision for two months. Neuro-ophthalmologic examination showed temporal pallor of right optic disc, combined pallor and edema of left optic disc; peripheral and central visual field defects of both eyes. Laboratory data, including spinal fluid examination, within normal limits. Roentgenogram of skull negative. Pneumoencephalogram showed a sharply demarcated obliteration of the cisterna chiasmatis and an encroachment upon the floor of the third ventricle. Diagnosis: suprasellar meningioma, verified.

in 4 cases (Fig. 1, 2, 3 and 4) in which the existence of a meningioma in the suprasellar region has been verified by operation and in another case (Fig. 5) where the presence of a hypophyseal duct tumor is highly probable.

In order to fully appreciate the diagnostic significance of obliteration of the cisterna chiasmatis in the pneumoencephalogram, it is necessary to briefly review the anatomy of this area and to correlate it with the appearance in pneumoencephalography. Schaeffer[9] has clearly shown that the exact position of the cisterna chiasmatis depends upon the anatomical position of the optic chiasm which may vary considerably in its relationship to the tuberculum sellae. His classical investigation also established the fact that the optic chiasm in 91 per cent of instances occupies a position directly

Fig. 3. Case III. C.W. (J.H. No. FH3327), female, aged twenty-three. History of increasing visual impairment of left eye associated with frontal headaches for three months and slight visual impairment of right eye for one month. Neuro-ophthalmologic examination showed slight pallor of left optic disc; inferior altitudinal visual field defect merging with a central scotoma on the left, and a central scotoma for color on the right. Laboratory data, including spinal fluid examination, within normal limits. Roentgenogram of skull negative. Pneumoencephalogram showed an obliteration of the cisterna chiasmatis. Diagnosis: suprasellar meningioma, verified.

above the diaphragma sellae while in another 4 per cent it is located above and posterior to the dorsum sellae. This anatomical fact permits one to consider the chiasmatic cisterna as including the basilar subarachnoid space above the sella turcica and overlying the diaphragma sellae. This

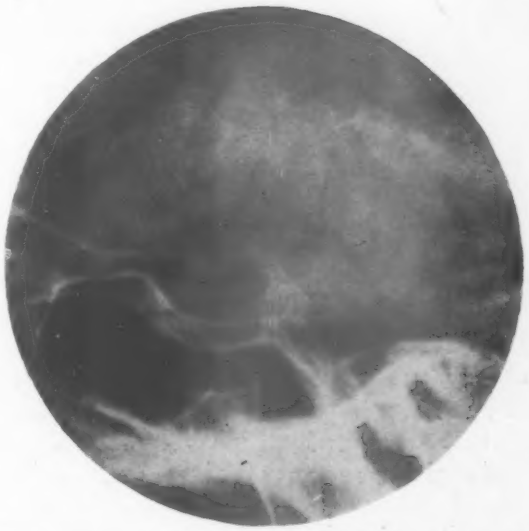

Fig. 4. Case IV. W. S. (J. H. No. HH13082), male, aged forty-four. History of impaired vision affecting the lateral half of the field of vision of the right eye for six weeks; impaired memory for about a year. Neuro-ophthalmologic examination showed pallor of both optic discs, more so on the right; slight proptosis of the right eye; temporal hemianopia of the right eye. Laboratory data within normal limits except for an increased spinal fluid protein of 130 milligrams. Roentgenogram of the skull negative. Pneumoencephalogram showed obliteration of the cisterna chiasmatis and a filling defect in the anterior portion of the floor of the third ventricle. Diagnosis: suprasellar meningioma, verified.

concept is in agreement with that expressed by Pancoast, Pendergrass and Schaeffer[7] who describe the cisterna chiasmatis as "located beneath and behind the chiasma —well portrayed as a rule just above the hypophysis." The cisterna chiasmatis communicates rostrally with the cisterna lamina terminalis and communicates caudally with the cisterna interpeduncularis.

A study of normal encephalograms with the anatomical definition of the cisterna chiasmatis as outlined above results in a 94 per cent visualization of this structure. This result was obtained in a control series of 150 consecutive pneumoencephalograms in which no lesion in the suprasellar region was suspected. It should be emphasized that for reliable visualization of the basal cisterns it is essential that there be adequate replacement of cerebrospinal

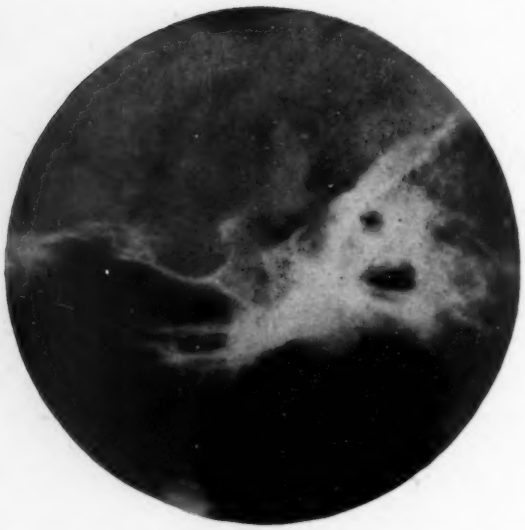

FIG. 5. Case v. J. G. (J. H. No. EH4554), male, aged nine. History of severe headaches for nine months and complete amaurosis for four months. Neuro-ophthalmologic examination revealed amaurosis and consecutive optic atrophy bilaterally; loss of pupillary reaction to light bilaterally; infantile habitus. Laboratory data, including spinal fluid examination, within normal limits. Roentgenogram of skull negative. Pneumoencephalogram showed complete obliteration of the cisterna chiasmatis with encroachment upon the cisterna interpeduncularis and cisterna pontis; upward and backward displacement of the third ventricle and anterior horns of the lateral ventricles. Diagnosis: suprasellar hypophyseal duct neoplasm, unverified.

fluid and that roentgenography be made in the erect posture. The size of the cisterna chiasmatis varies considerably (Fig. 6 and 7). Schaffer[9] reported an anatomic variation in depth from a potential space to a level of 10 millimeters.

Hypophyseal adenomas, hypophyseal duct neoplasms, and meningiomas are the tumors most commonly observed in the suprasellar region. Aneurysms of the internal carotid, anterior cerebral, and anterior communicating arteries are not infrequent. Gliomas of the optic chiasm are being reported in increasing number. Non-neoplastic lesions involving the primary visual pathways and, therefore, capable of producing a chiasmal or prechiasmal syndrome, include multiple sclerosis and retrobulbar optic neuritis. Optochiasmatic arachnoiditis (Fig. 8), as shown in a recent report by Pendergrass and Perryman,[8] is deserving of special attention in the differential diagnosis of suprasellar tumors since it is capable of obliterating the cisterna chiasmatis in pneumoencephalography and thus may not be distinguishable from a suprasellar tumor. However, the significance for the patient is more apparent than real since early diagnosis and neurosurgical treatment are desirable in both arachnoiditis and tumor cases.

Routine roentgen study of the skull will reveal quite variable findings in tumors in and around the sella turcica and optic chiasm. Hypophyseal adenomas which al-

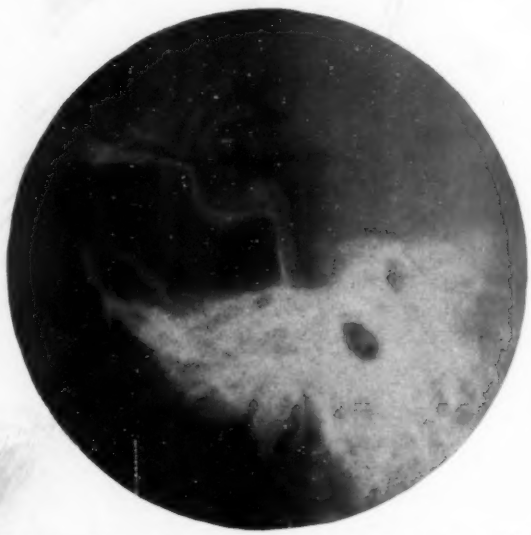

FIG. 6. Normal pneumoencephalogram in which cisterna chiasmatis is small and shallow.

most always arise within the sella turcica and subsequently spread into the suprasellar region will nearly always be easily identifiable by the characteristic ballooning of the sella. Hypophyseal duct neoplasms which nearly always originate in the suprasellar region may be identified in a very substantial percentage of cases by the calcification within the tumor and also may cause pressure effects downward upon the sella and clinoid processes. Parasellar tumors commonly show unilateral erosion of the sella and dorsum; a double sellar floor and unilateral clinoid erosion may be

present; the sphenoidal ridge and superior orbital fissure may show evidence of erosion. Meningiomas in the suprasellar region may produce hyperostosis of the tuberculum sellae in some cases. All of these tumors, however, if small, may produce no discernible alteration in the ordinary roentgenogram of the skull. This may even be the case with surprisingly large suprasellar tumors, especially meningiomas.

Pneumoencephalography was formerly considered least informative in tumors in the neighborhood of the sella turcica and optic chiasm. Too often with a negative roentgenogram of the skull and a presumably negative pneumoencephalogram, the

Fig. 7. Normal pneumoencephalogram in which cisterna chiasmatis is large and deep.

neurologist has had to decide for or against operation on the basis of clinical observation alone. Errors in judgment are not rare in this type of case. Therefore, it is felt that pneumoencephalography should be truly recognized as a highly accurate, informative, diagnostic procedure in the clinical investigation of suprasellar tumors. It is noteworthy that in Cases I and III (Fig. 1 and 3) obliteration of the cisterna chiasmatis constituted the only abnormal finding roentgenologically while in the other cases (Fig. 2, 4, 5) it was accompanied by encroachment upon the cisterna interpeduncularis and the floor of the third ventricle.

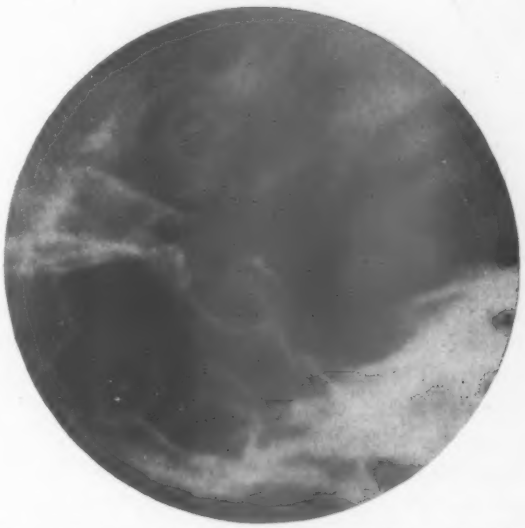

Fig. 8. Case VI. M. G. (J. H. No. BH8645), female, aged forty-eight. History of increasingly impaired vision for one year; periodic left temporal headaches for a year; sense of pressure in region of vertex for three weeks. Neuro-ophthalmologic examination revealed marked pallor of both optic discs; superior bitemporal, central scotomatous field defects combined with peripheral constriction of both visual fields. Laboratory data, including spinal fluid examination, within normal limits. Roentgenogram of skull negative. Pneumoencephalogram showed poor visualization of the cisterna chiasmatis and an absence of air in the subarachnoid pathways over both cerebral hemispheres with a normal ventricular system. Diagnosis: optochiasmatic arachnoiditis, verified.

It is suggested that in all patients who present the combination of visual impairment and prechiasmal or chiasmal visual field defects with or without headaches it is essential that the diagnostic investigation proceed in regular steps. If in such a patient routine roentgenograms of the skull and the spinal fluid examination fail to disclose significant information it is essential that pneumoencephalography be performed before the diagnosis of a suprasellar tumor is dismissed.

SUMMARY AND CONCLUSIONS

Tumors in the suprasellar region are frequently difficult to diagnose clinically. However, routine pneumoencephalography will

show obliteration of the cisterna chiasmatis in such tumors and permits their early detection. Five illustrative cases are described including four verified suprasellar meningiomas and one unverified hypophyseal duct neoplasm. A control study of one hundred and fifty consecutive pneumoencephalograms in which no suprasellar lesion was suspected shows 94 per cent visualization of the cisterna chiasmatis. Therefore, it is concluded that obliteration of the cisterna chiasmatis warrants the presumptive diagnosis of a suprasellar tumor, if a lesion in this area is clinically suspected. Conversely, clear visualization of the cisterna chiasmatis is sufficient to practically exclude the diagnostic possibility of a suprasellar tumor.

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RETROCARDIAC BRONCHIECTASIS*

By ROBERT G. BLOCH, M.D., LOUIS F. SANDOCK, M.D., *and* EARL B. MITCHELL, M.D.†
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THE importance of bronchiectasis among the pulmonary diseases has been increasingly recognized with the improvement of diagnostic procedures. Although the diagnosis of the extensive and advanced condition is usually suggested by history, symptoms and physical findings, the exact extent and location of the involvement can be ascertained only by the bronchogram, obtained by the endobronchial injection of iodized contrast oil. The now generally accepted fact that chronic bronchial dilatation is an irreversible process and curable only by surgical removal of the involved portions of the lung makes bronchographic examination mandatory as a guide in determining the operability of each case and the extent of the required surgical procedure.

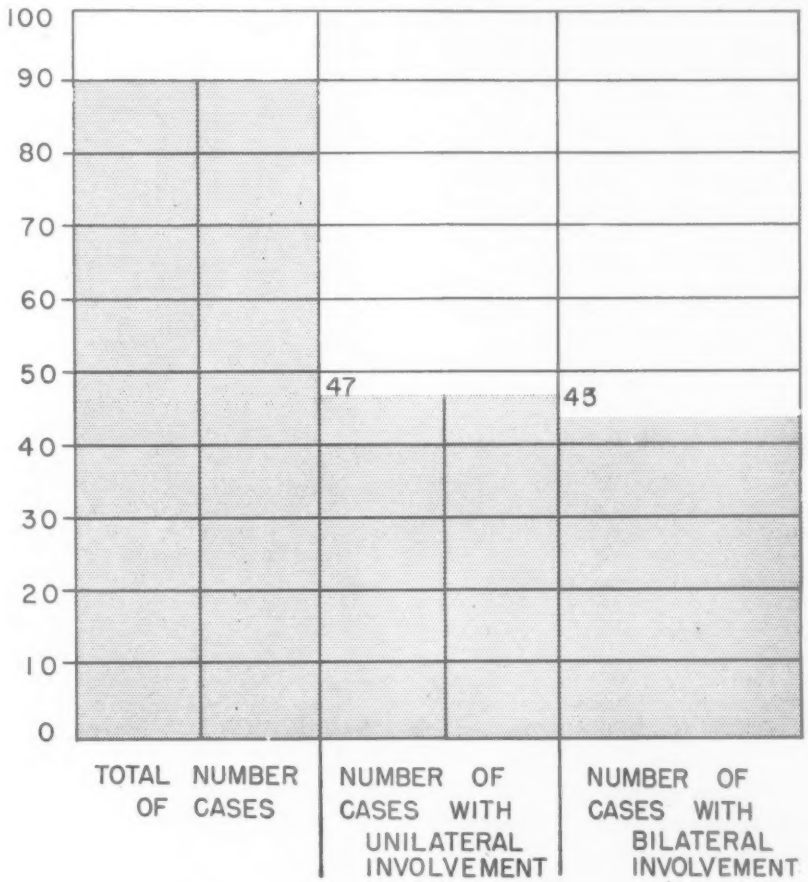

CHART 1

From bronchographic records thus accumulated, it is possible to point out peculiarities in the localization and distribu-

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† Now in Oakland, California.

tion of the disease to which only few authors have made reference in the otherwise voluminous literature on bronchiectasis.[1,2,3,4,5] We are referring to the observation that

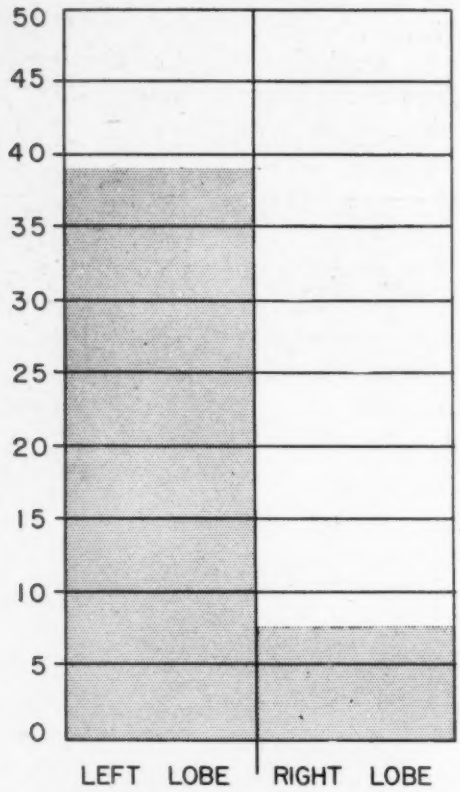

CHART II. Relative incidence of right and left lower lobe involvement.

there is a striking predilection of bronchiectasis for the lower lobe of the left lung. Unilateral involvement which was found in slightly over half of our series of 90 patients (Chart I) had affected the left lower lobe in the great majority of patients, namely in 39 out of 47, or 83 per cent (Chart II). No effort is made in this study to analyze the detailed lobar distribution of bronchiectasis. For the sake of brevity a small number of upper lobe involvements has been omitted as irrelevant for this discussion. Involvement of the right middle lobe usually associated with lower lobe disease has been included with the latter.

Classifying the degree of bronchiectatic involvement by an arbitrary scale of four grades, it was found that unilateral disease, too, occurred much more extensively in the left than in the right lung. Almost half of the left unilateral dilatations occurred in Grades III and IV, signifying extensive disease which was practically absent in patients with right unilateral findings (Charts IV and V). In bilateral disease also the left lower lobe was found more extensively involved than the lower portions of the right lung. Of 43 patients with bilateral involvement, 16 had about equally advanced disease, but 20, or 74 per cent, of the remaining 27 of that group had the left side more extensively affected than the right, often strikingly so (Chart III, Fig. 1). Application of the grade classification showed that the left predominant involvement in bilateral disease was generally in a more advanced state than were the right predomi-

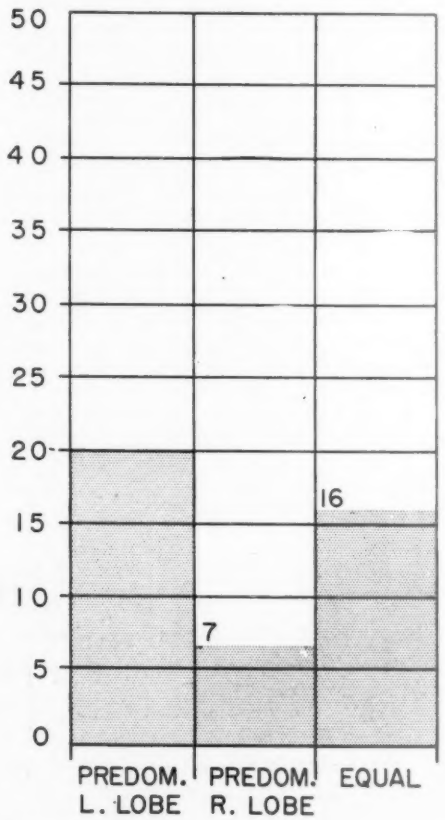

CHART III. Relationship of predominance in bilateral cases.

nant bilateral dilatations (Charts VI and VII). Whenever the extent of bilateral dilatations seemed to be equal in both lungs it was only rarely of the extensive variety (Chart VIII).

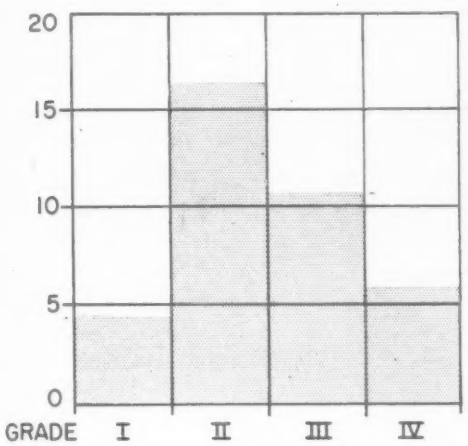

CHART IV. Extent of unilateral left lower lobe involvement.

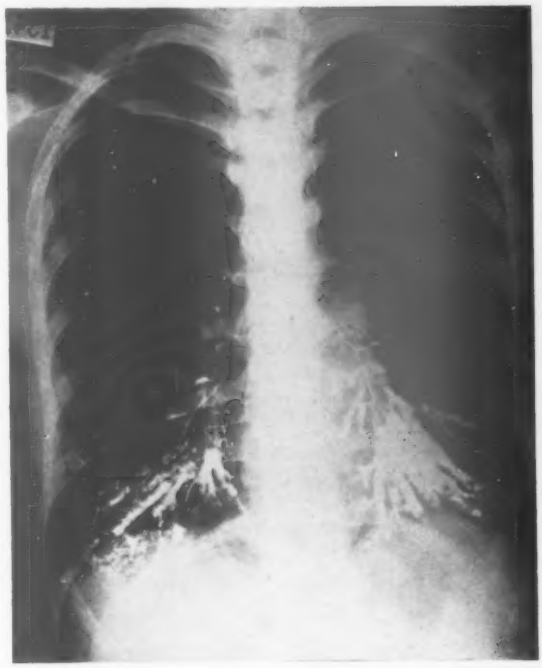

FIG. 1. Bronchogram of bilateral bronchiectasis showing the greater extent of the involvement in the left lung.

The most important diagnostic aspect of these observations lies in the fact that in routine roentgenograms of the chest, the greater part of the lung field representing the left lower lobe is obscured by the cardiac shadow. Therefore, the visible findings of bronchopulmonary involvement can be minimal and consequently pronounced bronchial symptoms may seem to be out of proportion with the roentgen evidence. Only the bronchogram can reveal the true extent of the disease (Fig. 2). Routine

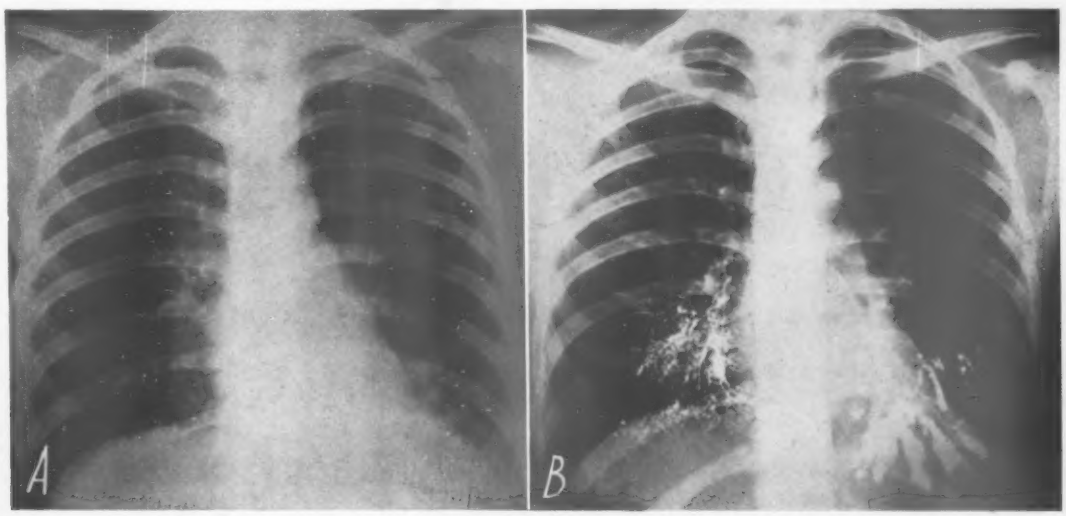

FIG. 2. Routine chest roentgenogram (*A*) showing minimal involvement in and near the left cardiophrenic angle. The bronchogram (*B*) shows the true extent of the disease in the retrocardiac area.

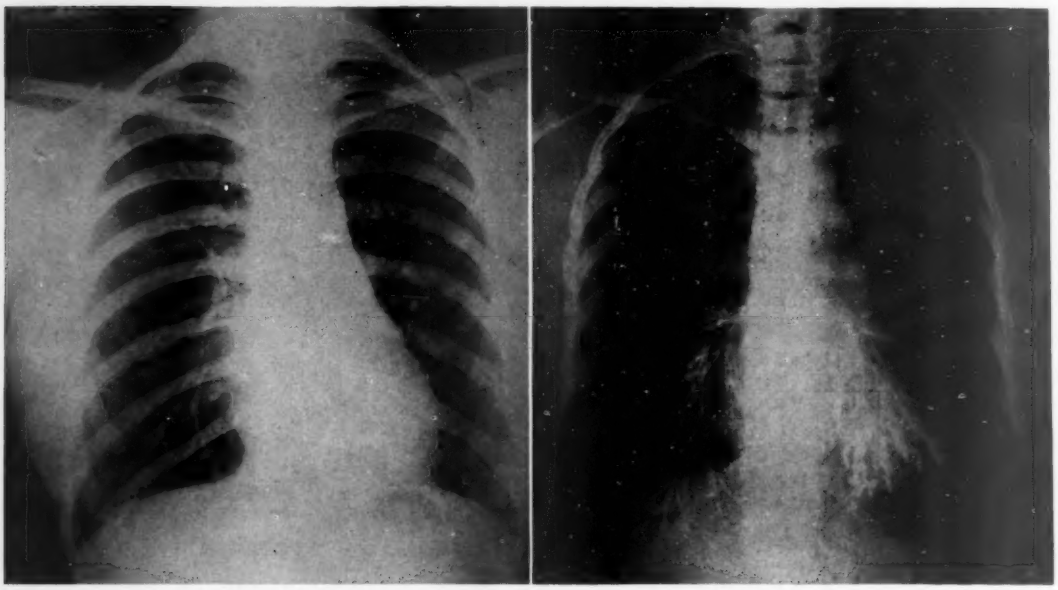

Fig. 3

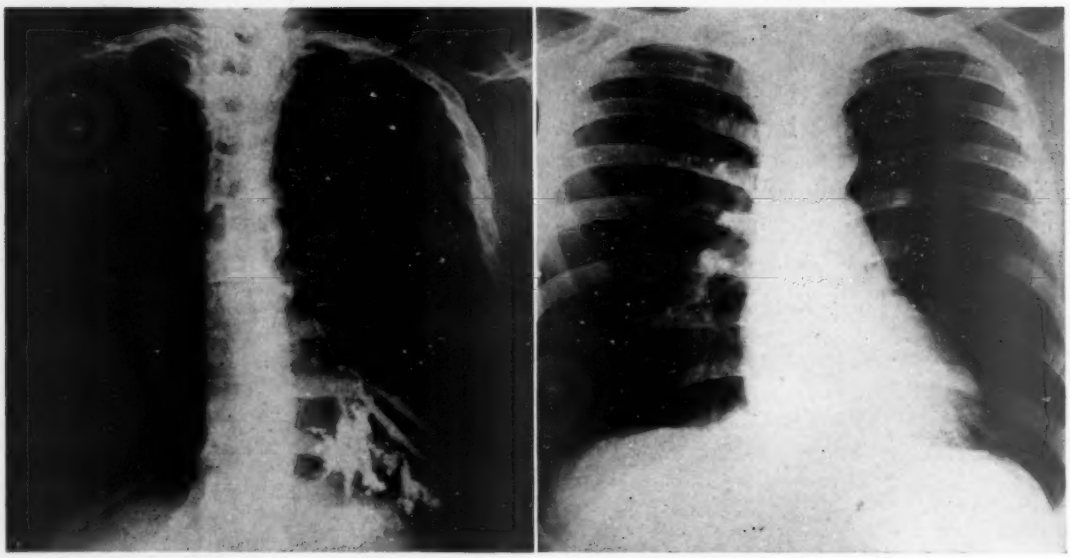

Fig. 4

Fig. 3 and 4. Essentially normal lung fields in the routine roentgenograms. The bronchograms show extensive bronchiectasis confined solely to the retrocardiac area of the left lower lobe.

roentgen findings in the lung field lateral to the heart shadow can be so minimal as to be easily overlooked, frequently they are non-existent.

Figures 3 and 4 illustrate extensive bronchiectasis confined solely to the retrocardiac area of the lung, demonstrable only by bronchography. Physical findings are more indicative of retrocardiac bronchiectasis than the routine chest roentgenogram although they may be scant in comparison with the severity of the involvement. Frequently they are interpreted as signifying a simple bronchitis, either acute or chronic. It is of great importance to keep in mind in this age of mass surveys that by

roentgen examination only a small percentage of patients suffering from retrocardiac bronchiectasis will be screened out. This was borne out by the experience with numerous cases among personnel in the armed forces[3] where eventually under the unaccustomed stress of the service the increase of symptoms, often recurrent pneumonias, called attention to a pre-existing bronchial dilatation.

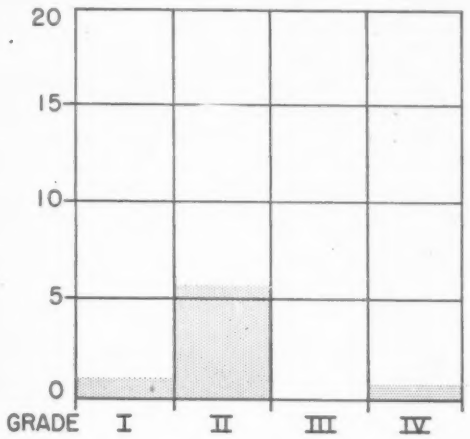

Chart v. Extent of unilateral right lower lobe involvement

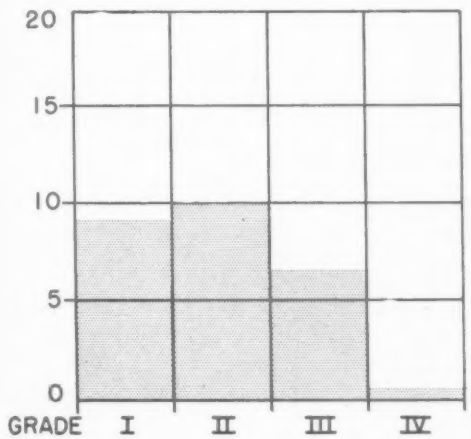

Chart vii. Extent of bilateral disease; predominance of right lower lobe involvement.

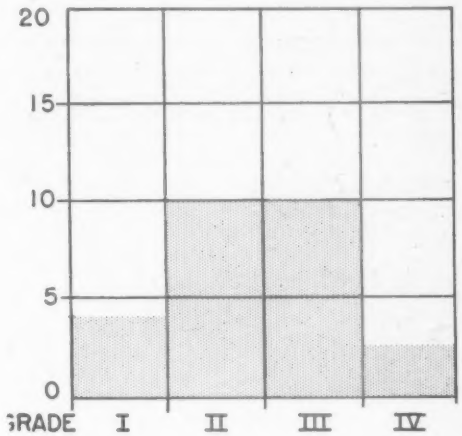

Chart vi. Extent of bilateral disease; predominance of left lower lobe involvement.

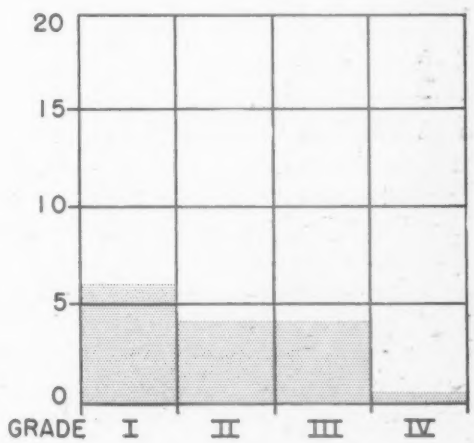

Chart viii. Extent of bilateral disease; equal involvement of both lower lobes.

The predominance of bronchiectasis of the left lower lobe and especially of the retrocardiac pulmonary area can hardly be explained by the configuration of the bronchial tree. We believe that it is the residual of more extensive bronchial disease in early childhood secondary to the variety of respiratory infections to which bronchiectasis can be attributed. Beginning bronchial dilatations may readjust themselves during the years of growth after the primary cause has disappeared, but the retrocardiac part of the involvement fails to do so because of the traction effect of pericardial adhesions which have resulted from the primary pulmonary infection. This traction can be assumed to be much aggravated by the action of the heart.

SUMMARY

1. Bronchiectasis involves the lower lobe of the left lung more frequently and

more extensively than any other pulmonary area.

2. The occurrence of unilateral bronchiectasis is nearly five times as frequent in the left as in the right lung.

3. Isolated bronchiectasis of the retrocardiac area of the left lower lobe is frequent. On routine chest roentgenograms it may escape recognition entirely and can be diagnosed only by bronchographic examination.

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SOME CLINICAL AND PATHOLOGICAL OBSERVATIONS IN A STUDY OF DEGENERATIVE ARTHRITIS OF THE HIP JOINT*

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CASES of degenerative arthritis which are classed as primary are actually instances in which the cause of the degeneration of the articular cartilage is not known. Some of these cases are apparently the result of senescence or wear and tear processes. In the secondary type, the degeneration of the articular cartilage leading to the development of an osteoarthritis has a known basis. Among the more common causes are untreated or inadequately treated Perthes' disease and slipped capital femoral epiphysis, congenital subluxation and dislocation of the femoral head, fractures into and about the hip joint, and aseptic necrosis of the head and neck of the femur from a variety of causes other than Perthes' disease (Fig. 1, *a* to *f*). Any condition which alters the anatomy of the hip joint will accelerate the appearance of degenerative changes incidental to wear and tear of function.

In a study of 81 cases of degenerative arthritis of the hip joint, of both the primary and secondary types, there were 16 in which the arthritis followed upon an aseptic necrosis of the femoral head. The degenerative arthritis was definitely engrafted on a pre-existing lesion of the hip joint in 48 of the 81 cases (59 per cent). Although some of the remaining 33 cases might very well be instances of the primary or spontaneous type, more adequate histories and previous roentgenograms might have excluded some as instances of the secondary type.

Tissue for histopathologic study was available in all of the 81 cases. The changes in the articular cartilage varies from fibrillation to complete erosion at the weight-bearing portions. Exostosis formation is a constant feature of the pathologic anatomy and contributes to the deformation of the bone ends of the joint. The subchondral bone trabeculae become compact and thickened, especially where the articular cartilage is eroded. The marrow of the femoral head becomes replaced in some areas by loose fibrous tissue and by the development of cyst-like cavities. Identical changes are present in the contiguous surface of the acetabulum (Fig. 2*a*).

The pathologic changes are visualized in the roentgenograms as follows: Thinning and loss of articular cartilage is demonstrated by loss of joint space. The thickened and condensed subchondral bone is manifested as sclerosis and there is a corresponding densification of the acetabulum. The cystic areas appear as subchondral areas of radiolucency (Fig. 2*b*). In those instances in which the head is enlarged it may protrude from the lateral confines of the acetabulum and in these cases an osteophytic ledge may appear at the lateral acetabular border. However, true subluxation of the femoral head may appear, the head being displaced laterally and the space between its medial surface and the acetabulum being filled in by the deposit of bone in the acetabular floor and by the medial beak of the enlarged femoral head (Fig. 2*c* and 3).

The combination of loss of articular cartilage over the weight-bearing portion of the head, deposition of bone at the head-neck junction and widening of the neck by actual periosteal bone formation in the neck region, produces a mushroom-like or cauliflower-like femoral head which is not unlike that observed in untreated or inadequately treated Perthes' disease or

* Work done under a Frederick Brown Research Fellowship in Orthopedic Surgery, Hospital for Joint Diseases, New York, N. Y.

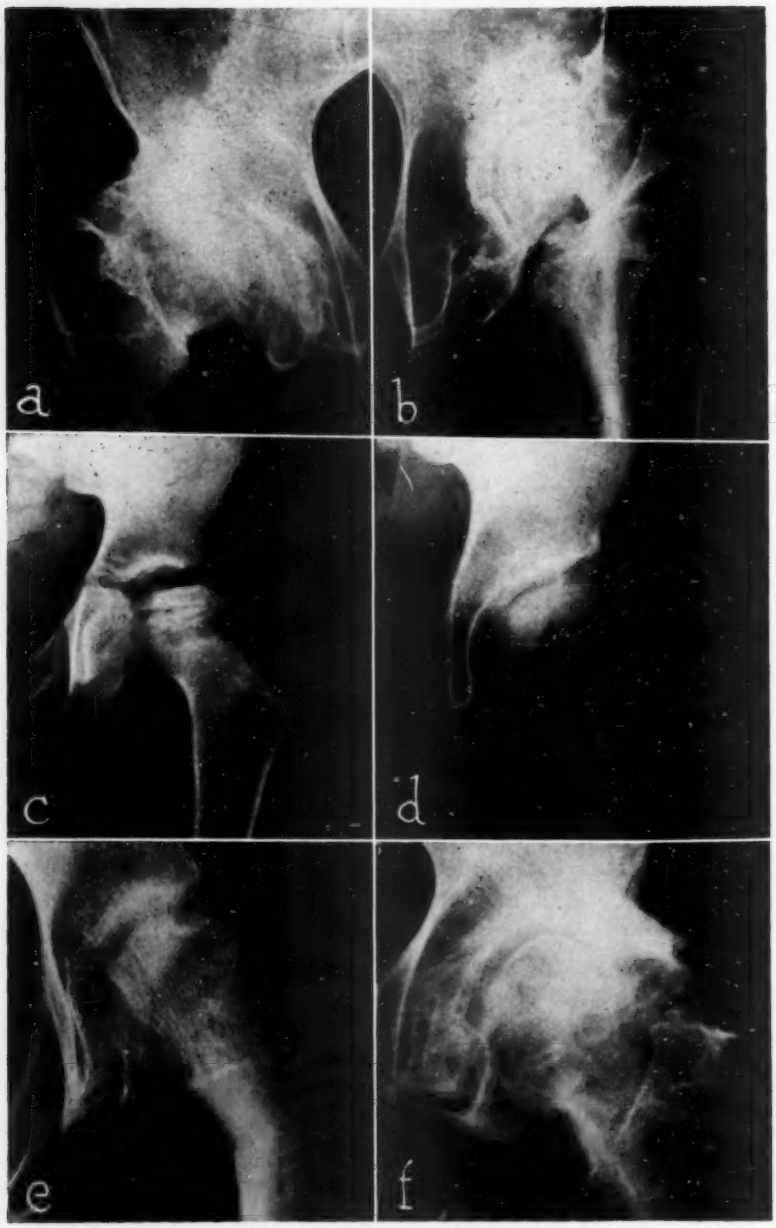

Fig. 1. Anteroposterior roentgenograms of (*a*) right and (*b*) left hip joints in a male, aged forty-five, with pain in both hip regions, more marked on the left side. The patient had been treated for a "limp" since childhood and he was told at the age of twenty that he had a congenital dislocation of the left hip. The right femoral head is subluxated, the acetabulum is defective and shallow, and there is an advanced secondary degenerative arthritis as manifested by loss of joint space, hypertrophy of the femoral head and subchondral osteosclerosis. The left femoral head is completely dislocated well above the original acetabulum. A large mass of bone on the medial aspect of the femoral head, the exact nature of which is more clearly defined in Fig. 2*d*, occupies the secondary acetabulum. Here the contacting bony surfaces are densely sclerotic and only a narrow joint space is visualized.

c. Anteroposterior view of the left hip joint in an eight year old boy showing early changes of Legg-Perthes' disease.

d. The same hip as in *c*, at the age of fifteen. There is a fairly pronounced flattening and mushrooming of the femoral head which now extends well out of the lateral confines of the acetabulum. The deformity

displacement of the capital femoral epiphysis (Fig. 2, *a* and *b*). The latter interpretation, however, should be made only following an evaluation of previous roentgenograms which demonstrate the evolution of the degenerative arthritis on the basis of these lesions (Fig. 1, *c*, *d* and *e*). Similarly, the shallow acetabulum, with or without subluxation of the femoral head, which is observed in some cases of degenerative arthritis, can be differentiated from a primary (congenital) dysplasia of the acetabulum only from an analysis of previous roentgenograms (Fig. 2*c*).

Avascular necrosis of the subarticular bone is not an intrinsic part of the pathologic picture in degenerative arthritis of the hip joint or of any other joint of the body. However, one of the most advanced manifestations of secondary osteoarthritis is found associated with aseptic necrosis of the femoral head (Fig. 2*f*). Aseptic necrosis of the femoral head and neck may follow upon traumatic dislocation of the head of the femur or fracture of the neck of the femur, with or without subsequent union. Indeed, the occurrence of aseptic necrosis and degenerative arthritis has been reported in a surprisingly high percentage of united fractures of the neck of the femur observed from one to two or more years after injury. Although necrosis has been observed to follow external fixation or internal fixation with equal frequency, the latter procedure, assuring a higher incidence of union and allowing earlier ambulation, may be followed by the early appearance of secondary deformity of the femoral head. In this respect, it is significant that an aseptically necrotic head undergoes no deformity in the presence of nonunion of a femoral neck fracture, when there has been little or no direct weight bearing on the affected side (Fig. 2*g*). Aseptic necrosis is also observed after sudden, marked displacements of the capital femoral epiphysis, in the bone ends and shafts in caisson workers (although identical changes have been observed in the femoral heads in persons who have never been caisson workers), and there are instances of "idiopathic aseptic necrosis" which develop on an obscure basis. That necrosis of the femoral head may occur, following sudden and severe displacement of the capital epiphysis, must be borne in mind when methods of treating displacement of the capital epiphysis are evaluated, especially in regard to the appearance of postoperative complications such as aseptic necrosis and degenerative arthritis.

In aseptic necrosis of the femoral head the nutrition of the articular cartilage becomes affected and a secondary osteoarthritis supervenes if the underlying bone is not replaced by normal bone, and, in cases of long standing, this osteoarthritis becomes greatly exaggerated with collapse and deformity of the femoral head. Pathologic fractures may occur between the dead and

has resulted from compression of the capital epiphysis, from lateral growth of this epiphysis over the neck superiorly, and from widening of the femoral neck due to actual periosteal bone deposition. This is quite unlike the deformity in degenerative arthritis of primary or spontaneous origin where the malformed head becomes greatly modified secondarily, by hypertrophic deposits especially at the head-neck junction. Note how the shape and depth of the acetabulum have become altered secondarily to conform to the outline of the deformed femoral head. Such a hip joint as is illustrated here must inevitably become the site of secondary degenerative changes as a result of malformation and incongruity of its bony components.

e. Anteroposterior view of the painful left hip in a sixteen year old boy. A moderate displacement of the capital femoral epiphysis had been treated at the age of thirteen by multiple drillings across the epiphyseal plate. The right femoral head had also been involved but had healed with minimal deformity and no residual pain. Histopathologic study of tissue removed at the time of arthrodesis of the left hip joint showed an advanced degenerative arthritis without any evidence of aseptic necrosis.

f. Anteroposterior view of the left hip in a fifty-six year old male with pain in both hip regions of ten years' duration. The osteoarthritis was equally advanced in both hip joints and this case is considered as a possible instance of degenerative arthritis on the basis of senescence or wear and tear processes. Histopathologic study revealed the changes of an advanced osteoarthritis and no evidence of aseptic necrosis.

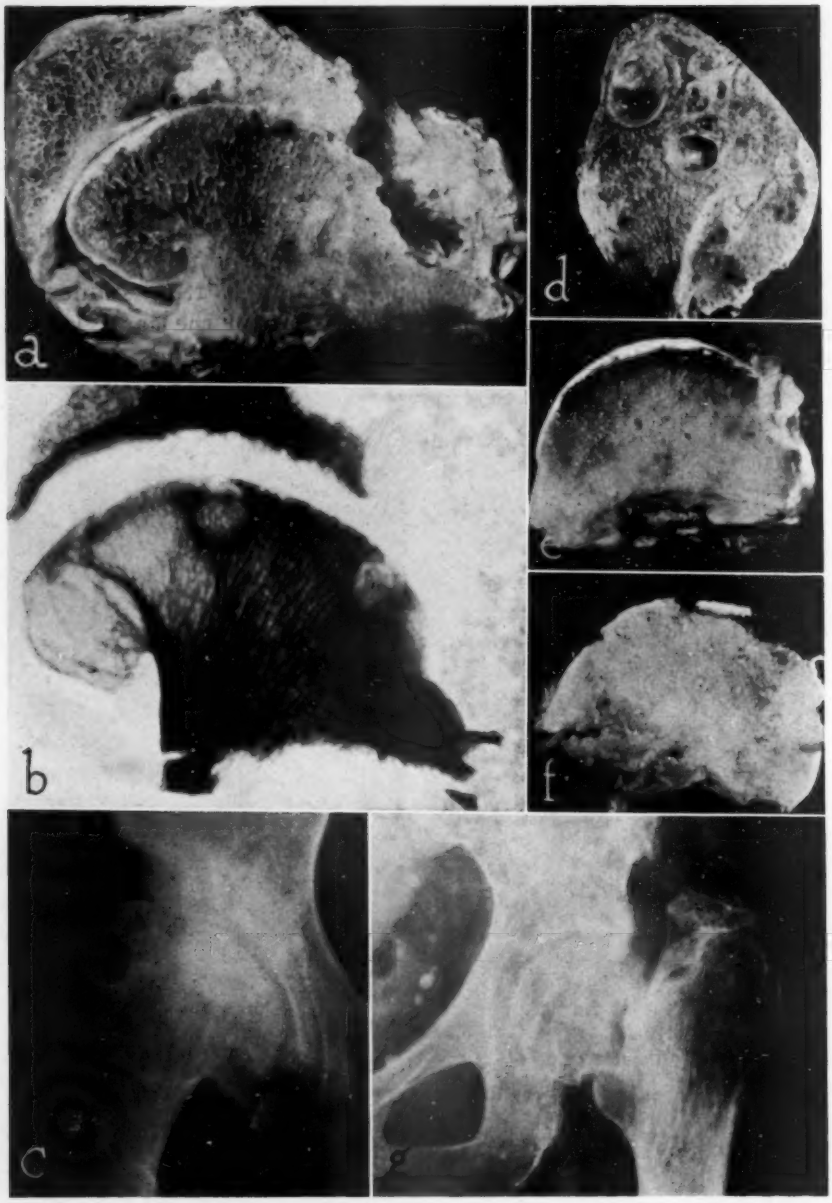

Fig. 2. *a.* Coronal section through the center of the right hip joint of a sixty year old female who died of melanomatosis and who gave a history of pain in the right hip of one year duration. The femoral head appears flattened, the joint space is narrowed and the articular cartilage is thinned, especially superiorly where the subchondral bone is densified. There are areas of fibrosis and cyst formation on the acetabular side and there is an enormous exostosis at the medial portion of the femoral head which contributes to its mushroomed appearance.

b. Roentgenogram of another coronal section of the specimen in (*a*). This shows more clearly the cystic areas in the femoral head and the large exostosis which extends medially beyond the thickened border of the femoral neck.

c. Anteroposterior roentgenogram of the right hip joint in a fifty-one year old female who had had a painful right hip for two years. The femoral head is enlarged and appears somewhat flattened. The joint space is markedly narrowed especially at its superior portion where the contiguous bony structures are densely sclerotic. There is a large radiolucent area in the lateral portion of the enlarged head which protrudes from the confines of the acetabulum. The enlargement of the head is due to bony deposition at the

living portions and result in collapse of the subchondral bone, delayed union and even in nonunion. The process of bone replacement may be "arrested prematurely" before its completion. For example, residual islands of dead bone have been observed many years after the clinical conclusion in Perthes' disease. For this reason even early recognition and the most judicious measures of protecting the affected areas may fail to prevent collapse and deformity.

In the writer's material, the head fragment in 2 cases of ununited fracture of the femoral neck, even though viable and without histopathologic evidence of aseptic necrosis, manifested secondary degenerative changes in the articular cartilage (Fig. 2*e*). The wisdom of exploring the hip joint so as to visualize the articular surface of the head fragment prior to reconstructive surgery becomes apparent. When this surface is extensively modified, those procedures which aim to preserve the femoral head are contraindicated and a procedure which entails removal of the head fragment or an arthrodesis appears to be in order.

The roentgenogram is not always a reliable method of interpretation in the diagnosis of aseptic necrosis. Necrotic bone will usually appear opaque in the roentgenogram as compared to the viable bone about it. Alterations in density result from atrophy of disuse, creeping replacement of dead bone by viable bone, pathologic fracture and collapse of dead bone bordering on joints, compression of dead trabeculae and infiltration of "bone sand" into the dead marrow spaces. However, should the process of resorption of the original bone keep pace with new bone formation, such sclerosis may not be evident. Indeed, there have been instances in my material in which the roentgenographic interpretation of the presence or of the absence of an aseptic necrosis has not been sustained by a thorough histopathologic survey of the tissue removed at the time of reconstructive surgery (Fig. 3*d*).

CONCLUSIONS

1. Degenerative arthritis may be classified as being primary or secondary. Those cases which are classed as primary are actually instances in which the cause of the degeneration of the articular cartilage leading to the development of an osteoarthritis is not known. Some of these cases, however, are apparently the result of senescence or wear and tear processes. In the secondary

head-neck junction. The acetabulum appears shallow in consequence of erosion at its superior border. The possibility of a pre-existing acetabular dysplasia could have been ascertained accurately only from roentgenograms made earlier in life.

d. Coronal section through the center of the resected femoral head and neck in a forty year old female with an unreduced congenital dislocation and with a history of pain for twelve years. The upper two-thirds of the specimen represents the original femoral head, now flattened and deformed. There is almost complete loss of the articular cartilage and there are marked alterations, including cystification, in the subchondral region. The lower third of the specimen represents an enormous exostosis formation and this had filled the original acetabulum.

e. Coronal section through the center of the femoral head fragment in a forty-three year old female with an ununited fracture of the left femoral neck of two years' duration. There is marked thinning and shredding of the articular cartilage, much fatty marrow in the head fragment and fibrous tissue at the site of nonunion. Microscopic sections revealed viable bone, no evidence of aseptic necrosis, and degenerative changes in the articular cartilage.

f. Coronal section through the center of the femoral head fragment in an elderly female with an ununited fracture of the neck of the left femur of about five years' duration. There is an advanced degeneration of the articular cartilage and a wedge-shaped area of aseptically necrotic bone.

g. Anteroposterior view of the left hip in a fifty-eight year old female who had sustained a fracture of the neck of the femur five years previously. The fracture is ununited and the neck is partially resorbed. Note that the contour of the head fragment is well preserved. Histopathologic sections of the excised capital fragment demonstrated an extensive aseptic necrosis and marked degeneration of the articular cartilage.

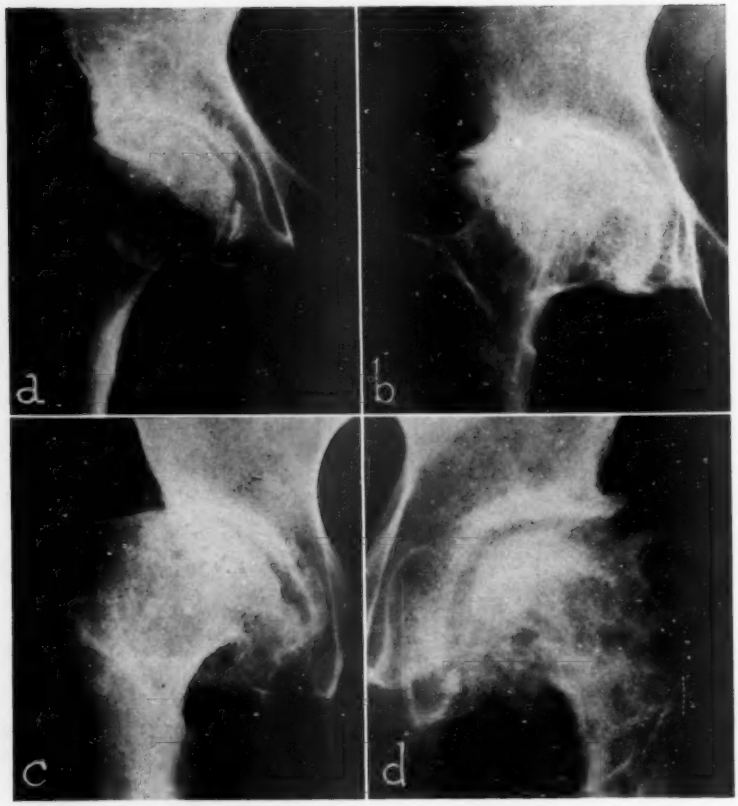

Fig. 3. Stages in the development of the roentgenographic features of degenerative arthritis as manifested by narrowing of the joint space, subchondral sclerosis and cystification, and marginal hypertrophy of the femoral head and neck and of the acetabular rim. Specimens removed at the time of arthroplasty in (*a*), (*b*) and (*d*), and arthrodesis in (*c*) showed the histopathologic changes characteristic of degenerative arthritis in all of these cases.

a. Anteroposterior view of the right hip joint in a fifty-four year old female with pain of three years' duration. There is beginning marginal spurring at the head-neck junction.

b. Anteroposterior view of the right hip joint in a forty-four year old female with pain of six years' duration. The femoral head is hypertrophied and there is a large spur at the superior margin of the acetabulum.

c. Anteroposterior view of the right hip in a forty year old male with pain of one year duration. There is marked proliferation of bone medially and laterally, creating an enormous femoral head which appears to extend from the confines of the acetabulum.

d. Anteroposterior view of the left hip joint in a forty-nine year old male with pain of fourteen years' duration. Deposition of bone at the head-neck junction in the form of a collar is more marked than in (*c*). The history of underground work as a coal miner for twenty years and later as a tunnel worker, and of the "bends" five years previously, and the patchy sclerosis of the head and neck suggested the possibility of an underlying or complicating aseptic necrosis, but this was not sustained by histopathologic study of all material removed at the time of surgical reconstruction.

type, the degenerative changes have a known basis.

2. In the development of the gross anatomical features in degenerative arthritis of the hip joint, the combination of loss of articular cartilage over the weight bearing portion of the femoral head, deposition of bone at the head-neck junction and widening of the femoral neck, produces a flattened, mushroom-type of deformity. The acetabulum may be shallow and the femoral head may appear subluxated. This deformity should be differentiated from the residual deformity in untreated or inadequately treated Perthes' disease or displacement of the capital femoral epiph-

ysis and congenital dysplasia of the acetabulum, with or without luxation of the head of the femur.

3. Although aseptic necrosis of the subarticular bone is not an intrinsic part of the pathologic picture in degenerative arthritis, one of the most advanced manifestations of secondary osteoarthritis is found associated with aseptic necrosis of the femoral head, arising from a variety of causes. The degenerative articular lesion in these cases becomes greatly exaggerated with collapse and deformity of the femoral head and this may even follow prolonged protection of the affected head when it fails to become fully revitalized. The occurrence of aseptic necrosis in the femoral head following sudden and severe displacement of the capital epiphysis must be borne in mind in the evaluation of methods for the treatment of this condition and its complications.

4. The diagnosis of aseptic necrosis from the roentgenograms alone is not always accurate. This is particularly significant in light of the attention now being focused on the aseptic necrosis and degenerative arthritis appearing one or more years following union of femoral neck fractures which have been treated by internal fixation. Degeneration of the articular cartilage of the femoral head may supervene even in the presence of a viable head fragment in fractures of the femoral neck, and this must be considered in selecting the most suitable reconstructive procedure for the treatment of delayed union and nonunion.

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HYPERTROPHIC OSTEOARTHROPATHY*

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SINCE the original report of Marie[17] and von Bamberger,[29] numerous articles regarding subperiosteal new bone formation have appeared in the literature. It has become obvious that this condition does not always result from primary involvement of the lungs. Although it is most common in pulmonary changes, it has been found in diseases of the heart, liver and blood, and recently a case was reported by Miller[21] showing typical changes of pulmonary osteoarthropathy secondary to a carcinoma of the thymus. Kline[14] recently had the opportunity of following a case of a young male with pulmonary and bone tuberculosis who developed a very extensive hypertrophic pulmonary osteoarthropathy.These changes have also been reported in the rat[27] dog,[3,11] horse,[2,15] and lion.[2] Most of the cases reported in dogs were secondary to pulmonary tuberculosis, but Wissing and Weisz[31] found its occurrence in a dog secondary to the presence of a highly malignant invasive bronchogenic carcinoma.

The study of this condition was stimulated by the admission of several patients to the hospital with the diagnosis of rheumatoid arthritis. They had been seen by physicians not connected with the hospital and had been treated for joint symptoms a considerable time without relief. There were no symptoms referable to the chest. Subsequent roentgenograms showed hypertrophic osteoarthropathy, thus strongly indicating the presence of an abnormal lung condition. This supposition was given in the roentgen report and in all cases proved to be correct. A review of the hospital records revealed several additional cases with identical stories. Craig,[6] in 1927, also reported 4 cases in which the pain and changes in the extremities led to the discovery of a pulmonary neoplasm. Holt and Hodges,[12] in their recent monograph, also called attention to the possibility of diagnosing longstanding chronic pulmonary or mediastinal disease by clinical and roentgen examination of the hand.

Previous literature on this subject is somewhat confusing as many of the cases listed under this entity have no histopathological proof. Many of the cases have only had simple clubbing of the fingers. Numerous investigators believe that clubbing and hypertrophic osteoarthropathy arise from the same causes, and that hypertrophic osteoarthropathy merely represents an advanced stage of the clubbing. Such reports include those of Locke[16] Mendlowitz,[19] Weens and Brown,[30] Fishberg,[7] Kessel[13] and Montgomery.[22]

Early reports indicated that tuberculosis and bronchiectasis were by far the predominating causes of hypertrophic osteoarthropathy. Recent reports show that carcinoma of the lungs is more prevalent. It is highly probable that the earlier cases which were thought to be tuberculosis or other conditions, were actually lung malignancies. As recently as 1938 Odessky and Shirshnev[23] reported a case of extensive subperiosteal new bone formation secondary to what he called a "catarrhal pneumonia." This pneumonia did not recede over a long period of time, and, in the roentgenograms which were produced with the article, there is a shadow which certainly suggests a bronchogenic carcinoma. If all patients with a diagnosis of carcinoma of the lung had roentgenograms taken of the extremities, the incidence of hypertrophic osteoarthropathy would undoubtedly be higher since this condition can be present without giving symptoms or signs.

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PATHOLOGICAL FINDINGS

Grossly, the process is essentially one of chronic proliferative subperiosteal osteitis surrounding the shaft of the bone, viz., tibia, fibula, radius and ulna, less frequently the humerus and femur or proximal portion of the phalanges. In the very advanced cases the clavicle, spines of the scapulae or vertebrae may be involved. The involvement is absent at the ends of the shaft where there is supposedly no periosteum. The new bone formation is from 1 to 7 millimeters thick and has a thin cortex surrounding the new cancellous bone which fills in the space between this new thin cortex just beneath the periosteum and the old cortex, which appears intact. This new bone formation is extremely vascular and there are recorded attempts at biopsy which have resulted in excessive hemorrhage and the necessity of packing before bleeding is controlled. This new bone is soft and pliable and easily cut or torn away from the old cortex. The clubbing of the fingers is said to be due, by most authorities, to soft tissue changes and there is no bone involvement. This consists of connective tissue thickening. Weens and Brown,[30] however, reported that absorption of the terminal phalanges may occur, and that these changes are preceded by hypertrophic changes. They illustrated cases where complete absorption of the unguinal process had occurred, giving the terminal phalanges the appearance of a thumb tack, and in some instances absorption had progressed so far that only the base of the terminal phalanx remained.

The joints are also involved. Some authors claim that nearly one-third of the cases have joint involvement consisting of a synovitis which may progress to actual erosion and ankylosis. Certainly the joints show extensive involvement clinically. Microscopically one can also see lymphocytic infiltration of the synovial membrane. The early microscopic changes consist of thin layers of new bone formation just beneath the periosteum which lie, layer on layer, surrounding the cortex of the original shaft. Perhaps six or more of these layers are distinguishable.

In the more advanced cases of this new bone formation the bone becomes firm but still presents a picture of a thickened bone surrounding the shaft with a thin, hard cortex just beneath the periosteum. No longer can distinct layers be detected, but it still remains quite vascular and, in the extreme cases, microscopically there has been reported erosion of the outer surface of the old cortex.

ROENTGENOGRAPHIC FINDINGS

These are exactly as one would expect from the above description of the gross changes and even the microscopic pathological findings. One question deserves comment—that of involvement of the terminal tuft of the fingers. Of the numerous cases of clinical description of clubbing of the finger, very few are recorded of actual flaring or mushroom appearance of the terminal tuft. After careful review of the literature and observation of routine roentgenograms of the fingers, it is our opinion that there are no bone changes in the terminal phalanges in this condition, and that the findings of lateral projection of the tuft can be seen in normal patients. We were unable to demonstrate any of the findings reported by Weens and Brown.[30]

THEORIES OF ETIOLOGY

Few of the very rare bone conditions have received as much attention as this disease. There are many theories, none of which satisfactorily explains the entire picture. Attempts to produce hypertrophic osteoarthropathy were universally unsuccessful. Von Bamberger placed material from a human lung abscess into the rectum of a rabbit; Compere, Adams and Compere[5] injected paraffin into the lungs of a dog and produced abscesses; Phemister[24] used various organisms intravenously while Harter and Churchill[10] tied off the bronchi in cats and monkeys. None of these experiments were successful in producing hypertrophic osteoarthropathy. Mendlowitz

and Leslie[20] anastomosed the left pulmonary artery to the left auricular appendage in four dogs. One developed hypertrophic osteoarthropathy while three did not. In the animal developing the hypertrophic osteoarthropathy, they were able to demonstrate an increased systemic blood flow. The purpose of their operation was to simulate the circulatory changes occurring in congenital heart disease with cyanosis. They thought that the chronic increased blood flow with increased periosteal nutrition was responsible for the proliferation of subperiosteal new bone.

Other theories varied from toxic absorption of infection within the chest to alteration of acid base equilibrium through decreased aeration as a result of compression of pulmonary vessels, constriction of the bronchi, lung compression or collapse. MacCallum,[18] in his textbook, agrees with the toxic theory in which absorption of poisonous material from the widened and infected bronchi is the cause of the changes in the extremities. Freund[8] reported a case of periosteal new bone proliferation without demonstrable pulmonary disease. The amount of bone production was markedly excessive, and occurred at the age of fourteen years. This author also believed the etiology to be toxic, but he was unable to find the source of the toxin. He thought it to be a proteinogenic substance which was not destroyed in the liver and entered the circulation and caused periosteal bone growth. He thought that this was a familial idiosyncrasy. He suggested this toxin might be related chemically to the product arising in various lung diseases which also became distributed throughout the body and reached the periosteum to lead to osteogenesis. Fried[9] analyzed 4 cases of hypertrophic osteoarthropathy in patients with bronchogenic carcinoma. Each of these cases showed pituitary dysfunction, and on the basis of data obtained, he believed that the bone changes were not caused by toxin or circulatory disturbance, but rather by endocrine imbalance, closely related to acromegalia and to pachydermia with pachyperiostosis. Campbell, Sacasa and Camp[4] postulated that the transference of oxygen from the blood is dependent upon the oxygen tension in the blood being less effective where the circulation is slow, as it is in the hands and feet. This decrease in oxygen tension was brought about by faulty aeration of the blood which passes through the lungs. This toxemia leads to edema where the circulation is slow, namely in the extremities.

In nearly all cases there is no clinical evidence of obstruction to the venous return of the blood, but rather, according to Campbell, there is "a varying amount of lung tissue which has ceased to fulfill its proper function." This seems highly improbable in view of the fact that a circular or peripheral carcinoma of the lung, only 4 or 5 centimeters in diameter, is capable of producing marked bone and soft tissue changes, the symptoms of which can be promptly relieved by a pneumonectomy. It is obvious that there has been a marked reduction in the amount of lung tissue remaining following the operation when compared with the area involved by the tumor itself. It is, however, difficult to think that anything except immediate improvement of circulatory conditions could be responsible for such a rapid improvement in clinical symptoms. Prompt and complete disappearance of the symptoms after a pneumonectomy was seen in 1 of the cases to be reported, and disappearance of the symptoms following radiation therapy in 2 other patients. Van Hazel[28] reported prompt relief of symptoms in 1 of his patients who had been bed-ridden for six months, following the removal of a benign intrathoracic neurofibroma. He also cited 12 cases from the literature where rapid improvement followed excision of a thoracic tumor, lobectomy or pneumonectomy. Several authors have expressed the opinion that at least two factors are necessary to produce the secondary osteoarthropathy, namely, a toxemia from long-standing disease and circulatory disturbances resulting from either cardiac or pulmonary involvement. Harter

believed that the condition was due to lack of oxygen, and called attention to the somewhat similar changes found in some people living at high altitudes where oxygen is rare. This observation seems significant.

Locke[16] did not believe that uncomplicated heart disease was capable of producing periosteal new bone formation. He was unable to find any cases in the 144 that he described, his own and those reported from the literature. He stated that "in view of the high incidence of heart disease and the care with which it is studied throughout the world, it seems significant that no cases of uncomplicated heart disease with clubbed fingers have had periosteal new bone formation roentgenographically demonstrated." He believes that "if the combination is not truly non-existent it must be at least extremely rare." Holt and Hodges[12] state that pulmonary osteoarthropathy occurs more frequently in non-tuberculous cases and that they were unable to find a single instance of its occurrence in uncomplicated pulmonary tuberculosis in the case records of the University Hospital.

CASE REPORTS

Case I. M. O., female, aged fifty-three, was admitted to the hospital with a chief complaint of stiffness of the hands and knees of four months' duration. She had been referred by her local physician, who was a prominent arthritis specialist, because of joint symptoms. She had developed progressive swelling, stiffness and pain in the ankles, knees and hands. Later the wrists became involved. The pain was not too severe but there was considerable limitation of motion. She received one gold injection without relief. There was a 20 pound weight loss and considerable weakness.

Her past history and family history were unimportant.

Physically, she appeared to be chronically ill. The extremities presented swelling of the hands so she was unable to make a fist. The wrists were swollen and stiff. The knees and ankles were also swollen, tender and edematous.

The clinical impression was rheumatoid arthritis.

Blood count revealed a secondary anemia.

Roentgenograms of the extremities were ordered. These showed evidence of periosteal proliferation along the shafts of the long bones. The impression was that of a Marie Bamberger syndrome and a chest roentgenogram was recommended. This showed a previously unsuspected circular shadow in the left upper lobe with a pleural effusion. The impression was that of a bronchogenic carcinoma.

A bronchoscopic examination showed slight displacement of the trachea.

She was given a course of deep roentgen therapy to the tumor mass which resulted in regression of the tumor, and there was a considerable improvement in the symptomatology attributable to the hypertrophic pulmonary osteoarthropathy. She was discharged, but returned to the hospital eight months later with evidence of extensive metastases. Thoracentesis showed malignant cells in the pleural fluid. She died at home after a retrogressive course.

Case II (Fig. 1 and 2). E. D., male, aged fifty-two, was admitted to the hospital with a chief complaint of pains in the joints for a year and a half. He had first noted swelling of the ankles that later became painful. The knees then became involved and the ankles improved. However, other joints subsequently became involved and were painful and swollen. There was also blurring of vision and a 30 pound weight loss occurred. He also was treated by a local physician for a progressive arthritis. At no time were there any symptoms referable to the lungs.

Fig. 1. Case II. There is marked periosteal proliferation along the shafts.

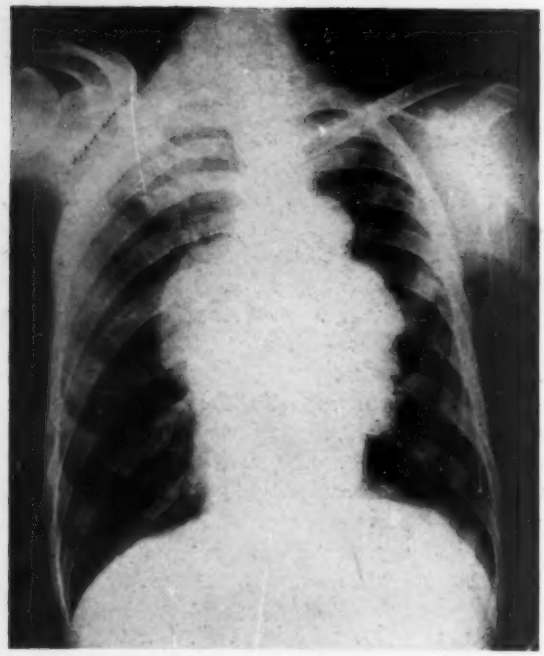

Fig. 2. Case II. There is a large mass with scalloped margins suggesting tremendously enlarged nodes.

Physically, the patient appeared to be cachetic. There was a right lateral proptosis. Examination of the chest revealed dullness anteriorly on the left with rales at the bases. The left leaf of the diaphragm was fixed. The heart was enlarged. The liver was enlarged. The fingers showed terminal clubbing. There was soft tissue proliferation about all the joints. These were tender.

A chest roentgenogram showed a very large mediastinal mass, thought most likely to be a lymphosarcoma with tremendously enlarged nodes. Roentgenograms of the extremities showed marked periosteal proliferation of all long bones. There was destruction of the terminal phalanx of the left thumb due to metastasis.

A course of deep roentgen therapy was given to the chest on the presumption that this was a lymphosarcoma. There was no response to therapy. The left thumb was disarticulated and the pathologist reported metastasis due to undifferentiated bronchogenic carcinoma. The patient's condition became very poor and he was discharged for terminal care.

Case III (Fig. 3, 4 and 5). N. A., male, aged forty-four, complained of swelling and pain in the joints of nine months' duration. He first noticed pain, swelling of the ankles, knees, toes, fingers and wrists. His local physician made the diagnosis of rheumatic fever. He was treated on this basis and some improvement of symptoms occurred. Movement improved, but the pain persisted. About ten weeks before admission to the hospital, there was sharp pain in the interscapular region. He was admitted to another hospital where the first chest roentgenogram was made. This was interpreted as a "lung infection." An operative procedure was performed but the results were unknown to us. No relief was obtained. At the time of admission, joint pain was considerable and the back

Fig. 3. Case III. The joints were swollen, tender and stiff. The periosteal proliferation is extremely marked.

pain was related to respiration. There was a weight loss of 40 pounds.

On physical examination, the patient appeared to be poorly nourished and chronically ill. There were palpable nodes in the axillary and inguinal regions. There was a well healed incision over the medial border of the right scapula. Dullness was elicited over the right chest anteriorly. Breath sounds were diminished. All fingers and toes showed evidence of marked clubbing. The wrists, knees and ankle joints were swollen.

Roentgenograms of the chest showed a large,

soft tissue mass, approximately 11 cm. in diameter, associated with atelectasis of the right upper lobe. There was right pleural effusion. Roentgenograms of the extremities

Fig. 4. Case III.

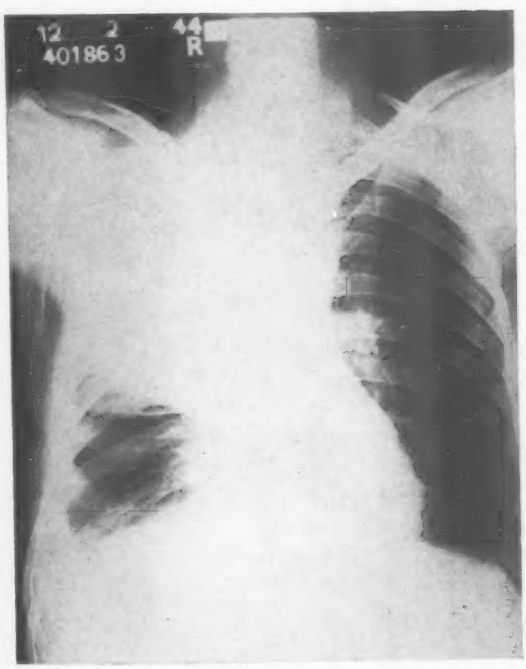

Fig. 5. Case III.

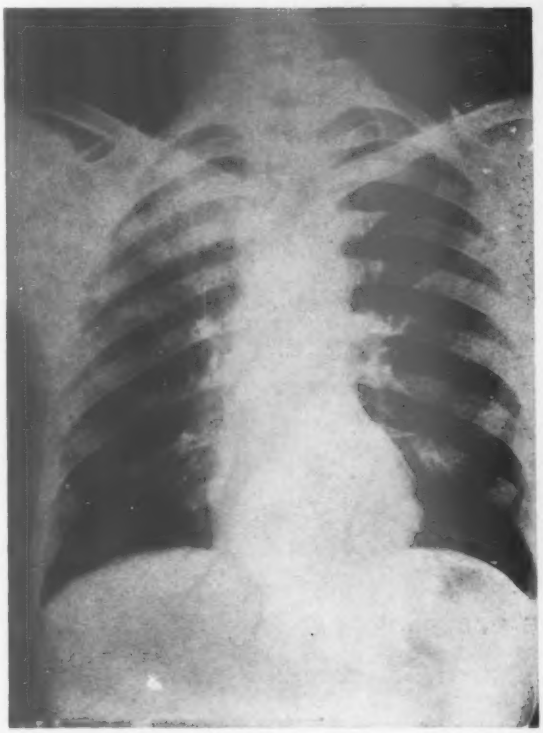

Fig. 6. Case IV. There is a large round mass in the right upper lobe which was proved to be a bronchogenic carcinoma.

showed extensive periosteal, new bone formation.

A biopsy of a right supraclavicular node showed a metastatic mucous adenocarcinoma. Bronchoscopic examination revealed extrinsic pressure on the trachea.

The patient was treated with deep roentgen therapy but without any beneficial effect. He was then discharged to a home for incurables.

Case IV (Fig. 6, 7 and 8). E. S., male, aged fifty-six. This patient first noted clubbing of his fingers which was followed several months later by pain in the hips. Just before admission the pain became extreme, and involved the knees, which became hot, tender and swollen. There was disability of the hands, fingers, wrists ankles and toes. There was also pain in the right anterior lower chest. This, however, did not occur until late in the disease. This patient was seen by an outside physician and was being treated as a case of rheumatoid arthritis with gold therapy. A routine chest roentgenogram showed a mass in the right upper lung field. At this time there were still no symptoms referable to the chest, but shortly after, there was pain

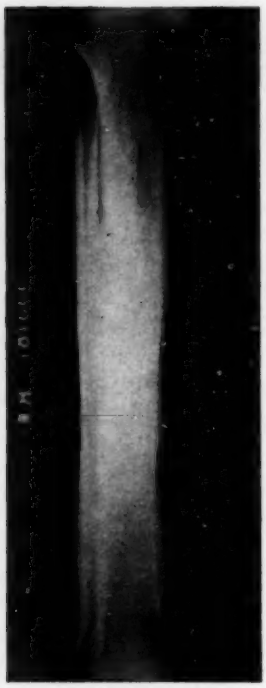

Fig. 7. Case IV. The periosteal new bone formation involves the entire lengths of the shafts.

Fig. 8. Case IV. The joints were very tender. The patient was being treated for rheumatoid arthritis. The metatarsals show periosteal proliferation.

associated with a cough and sputum. Subsequent workup in the hospital demonstrated a carcinoma of the right upper lobe. A right pneumonectomy was performed. Before operation, roentgenograms of the long bones showed hypertrophic, pulmonary osteoarthropathy of the long bones of the hands and feet.

The patient made an uneventful recovery from the operation, but later he was readmitted because of pain in the right shoulder. Roentgenograms of the extremities showed some improvement in the appearance of the pulmonary osteoarthropathy. He was discharged and did quite well for several months. He was again admitted the third time because of very severe pain in the right shoulder and radiation down the right arm. On physical examination, there were massive metastatic cervical lymph nodes as well as nodes in the left axilla. A chordotomy and posterior root section from the 1st to the 6th cervical vertebra were performed. The patient died on the sixth postoperative day.

Case V (Fig. 9 and 10). O. T., aged fifty-one, was referred from another institution because of a bad taste in the mouth, nausea and vomiting. His father died of tuberculosis and his mother of Bright's disease. He had had pneumonia in 1918 and malaria at the age of eigh-

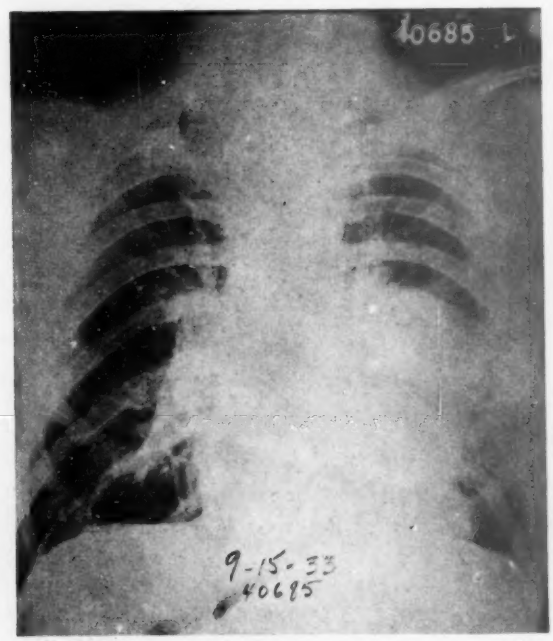

Fig. 9. Case V. There is a large, rounded mass in the left hilar region. A surgical defect of the left ninth rib is present.

teen. There was a history of a luetic and neisserian infection in 1898. Several years before admission, the patient began to suffer with swelling, stiffness and in pain the right knee and ankle, and to a lesser degree in the left. There was some fever. A tonsillectomy was performed, following which the patient complained of a bad taste in his mouth and a foul breath. There was no symptoms referable to the chest, but there was a weight loss of 40 pounds. His serological test was found to be positive and anti-luetic therapy was started. There was slight improvement, but the symptoms soon recurred, for which the patient was re-admitted to the hospital. A routine chest roentgenogram was made at this time and what was thought to be an encapsulated empyema was seen. A thoracotomy was performed but no evidence of pus was obtained. The surgeon thought he was able to palpate a mass. Subsequent roentgenograms showed a definite mass in the left lung. He was then referred to the New York Hospital. At the time of admission, he was both acutely and chronically ill. The ankles were swollen and painful. The toes and fingers were clubbed. Coarse and medium rales were heard over the lower half of the left lung. There was a moderate anemia. The Kline reaction was 4 plus. A chest roentgenogram showed a fairly well circumscribed mass, thought to represent a new growth. A surgical defect of the left ninth rib was seen. Roentgenograms of the extremities revealed periosteal proliferation of the tibiae, fibulae and the third, fourth and fifth metacarpals, due to hypertrophic pulmonary osteoarthropathy. Bronchoscopy was performed and a partial obstruction of the left main bronchus was found. It was thought the patient had an inoperable carcinoma of the left lung. He was discharged and died two months after leaving the hospital.

Fig. 10. Case v. Both bones show periosteal proliferation.

Fig. 11. Case vi. There is a large round dense shadow which increased in size despite all forms of therapy.

Case vi (Fig. 11 and 12). D. K., male, aged seventy-three. The patient was first seen in 1932 complaining of pain in the left shoulder and swelling of the hands and ankles. The pain had started two months before and was associated with weakness and tiredness. He was admitted to another institution because of pain in the extremities and joints. A chest roentgenogram showed a large mass in the right upper lobe. Biopsy was refused. He was uncooperative and, after receiving an undisclosed amount of roentgen therapy, he was discharged. The pain in the bones and joints was interpreted as

Fig. 12. Case VI. There was clubbing of the fingers. The periosteal new bone formation is best seen along the proximal phalanges.

metastases. On admission to the New York Hospital, the patient had pain in the right chest, knees and ankles. Just previous to admission there was occasional bood-streaked sputum. There was considerable weight loss. On examination, tenderness was present over the right upper lobe. Breath sounds were distant. There were rales at the right base. The distal phalanges showed early clubbing. There was edema of the feet and lower legs. A chest roentgenogram revealed a large, round, fairly well circumscribed shadow in the right mid-lung field, approximately 7 cm. in diameter. Later films showed gradual enlargement of the mass. Roentgenograms of the hands showed evidence of periosteal proliferation along the proximal phalanges of the hands suggesting hypertrophic pulmonary osteoarthropathy. Further deep roentgen therapy was given to the right chest, but the patient became progressively worse and was discharged to a home for terminal care.

Case VII. J. H., male, aged thirty-seven, was first seen because of pain in the right shoulder. This had started ten weeks before admission and was associated with slight cough and sputum. The pain gradually increased in intensity, and required narcotics for relief. Drooping of the right lid occurred with increased sweating on the left side. Clubbing of the fingers and toes was noted during this interval. On physical examination the patient appeared to be acutely ill and showed evidence of marked weight loss. There was ptosis of the right lid with right-sided anhidrosis. There were no abnormal findings in the chest. The extremities showed marked clubbing. A chest roentgenogram showed a homogeneous density within the circle of the right first rib. The inferior portion of the fourth rib showed destructive change. The impression was that of a bronchogenic carcinoma. The long bones showed minimal periosteal new bone formation involving the radii, tibiae, fibulae and left ulna. Bronchoscopy was negative.

A pneumonectomy was performed and resection of portions of the right third, fourth and fifth ribs were done. The pathological diagnosis was pleomorphic carcinoma of the right upper lobe. The patient received roentgen therapy postoperatively. A total of 2,400 r, measured in air, was given to the right chest posteriorly. The patient was then discharged.

Case VIII (Fig. 13 and 14). J. P., male, aged fifty-four, came to the clinic complaining of pain in the chest and legs of nine months' duration. The symptoms first started with a stabbing pain in the left chest which radiated both anteriorly and posteriorly. This gradually increased in intensity. Appetite was poor. There was a sensation of pressure in the chest. The pain then began to radiate down the left arm, and the left hand swelled. The finger nails became curved. The left knee and ankle were very painful and then both left extremities were weak. About a month before admission the right hand showed changes similar to the left. There was a 40 pound weight loss. Examination showed the patient to be chronically ill. The teeth were dirty and carious. Gingivitis was present. The lungs were clear. The breath sounds in the left paravertebral between the fourth and sixth dorsal vertebrae. The spine was tender between the first and fourth dorsal vertebrae. The sounds were distant. No murmurs heard. Bilateral inguinal hernias were present. The extremities showed marked club-

bing of the fingers and toes, with involvement of the hands and feet. A chest roentgenogram revealed increased markings suggesting bronchiectasis with pulmonary emphysema. A curvilinear calcium line was seen in relation to the left hilum. A second chest roentgenogram made three days later was interpreted as an air-filled cavity adjacent to the left hilum with a calcified shell—probably a bronchogenic cyst. Roentgenograms of the upper extremities showed typical changes of periosteal bone proliferation. Barium enema and gastrointestinal series were reported as negative.

The patient was seen by an ear, nose and throat consultant who found fixation of the left vocal cord. Bronchoscopic examination showed edema of the main bronchi. There was no evidence of a tumor. Urological findings were normal. During the latter part of his stay, the patient developed a left upper lobe pneumonia which responded to chemotherapy. Because of persistent chest pain, a course of deep roentgen therapy was tried; 1,600 r, measured in air, was given to two portals without effect. He was discharged but failed to return for follow-up. The case remained undiagnosed but was thought to be a bronchogenic cyst.

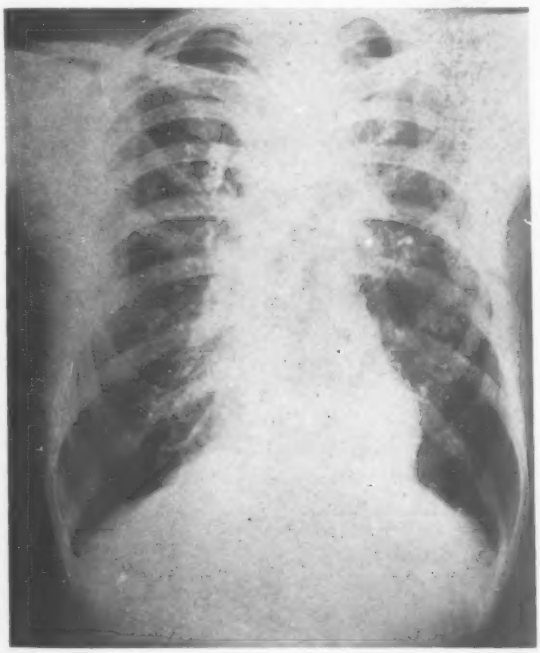

Fig. 13. Case viii. There is bilateral pulmonary emphysema. The markings are increased, suggesting bronchiectasis. A curvilinear calcium line is seen adjacent to the left hilum. It was interpreted as a bronchogenic cyst.

Fig. 14. Case viii. The periosteal proliferation involves mainly the metacarpals.

Case ix. J. H., male, aged fifty-one, was first seen in the clinic in 1933, complaining of weakness and swelling of the ankles and poor appetite. He had these symptoms since 1929, for which he had been admitted to another hospital. His case was diagnosed as Addison's disease and chronic pulmonary tuberculosis. He improved and was asymptomatic until 1933, when his symptoms returned. The weakness was associated with a weight loss of 20 pounds, and stiffness of the knees and ankles. There was moderate dyspnea on exertion. The fingers had always been clubbed. While being observed in the Out-Patient Department, a lump was noted in the left breast. He went to a city hospital and a radical mastectomy was performed. No report was received from this institution as to their findings.

On physical examination, the patient presented marked emphysema of the chest. There were a few rales at the left base. The left

breast was absent. There were no murmurs. The extremities showed clubbing of the fingers and toes. The ankles were very large. The ankle joints were stiff.

Roentgenograms of the chest revealed old, bilateral, apical scarring. There was no evidence of scarring. Bronchography showed a small area of bronchiectasis in the posterior left lung field. The roentgenograms of the long bones showed generalized, periosteal proliferation indicating the presence of hypertrophic, pulmonary osteoarthropathy.

The patient was discharged to be followed in the Pulmonary Clinic. He showed no improvement over several years and was lost sight of. It was later reported that he died in April, 1940.

Case x (Fig. 15 and 16). V. G., male, aged sixty-eight, was referred to the Out-Patient

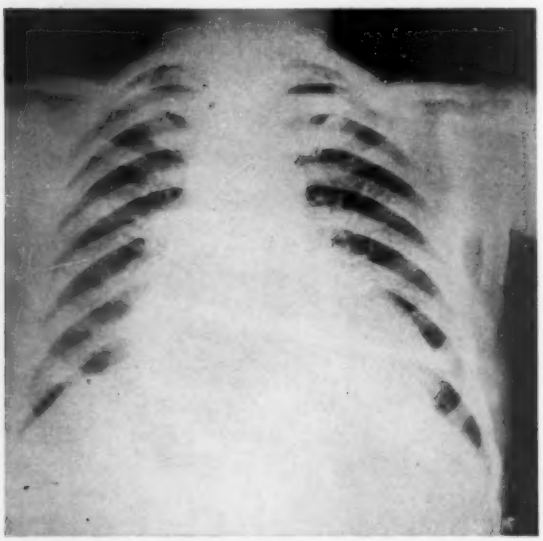

Fig. 15. Case x. There is generalized enlargement of the heart with congestive changes. The lung parenchyma is clear.

Department by his local physician because of a markedly enlarged spleen and shortness of breath. Five years before admission, the patient had an attack of pneumonia, for which he was hospitalized at another institution. His blood count at that time showed the usual leukocytosis, but there was no evidence of abnormal cells. In 1941 he again entered another hospital where he was again treated for a pneumonia and hypertensive heart disease. Blood counts were consistent with the usual changes in a pulmonary infection. It was about this time that he first noted a mass in the upper left quadrant. He was first seen in the Out-Patient Department of the New York Hospital in January, 1942, complaining of dyspnea, weakness, palpitation and edema. The liver and spleen were found to be enlarged. The blood count was that of a chronic myelogenous leukemia. The total white blood count was 100,000. Differential showed 5 per cent lymphocytes, 1 per cent monocytes, 4 per cent eosinophiles, 4 per cent basophiles, 9 per cent mature polymorphonuclears, 35 per cent band forms, 16 per cent metamyelocytes, 11 per cent myelocytes, 12 per cent promyelocytes, 5 per cent myeloblasts. Hemoglobin 52 per cent. Red blood cell count was 3.75 million. Kline test was negative. Urine showed a 3 plus albumin. Smears for malaria were negative.

The physical examination showed marked generalized wasting. Hard, shotty nodes were present in the axillary, inguinal and posterior cervical regions. The heart was enlarged and systolic, apical murmurs could be heard. The spleen was tremendously enlarged and reached well into the pelvis. The liver was palpable 4 fingerbreadths below the right costal margin.

A chest roentgenogram was reported as marked, generalized cardiac enlargement with congestive changes. A film of the right femur showed a thickening of the periosteum due to chronic pulmonary osteoarthropathy.

Fig. 16. Case x. The entire periosteum is thickened.

The patient was given three series of deep roentgen therapy over the spleen, resulting in a considerable reduction in the size of the spleen. He improved after each course, but the symptoms recurred. He ran a gradually retrogressive course but eventually did not return to the clinic.

Case xi (Fig. 17 and 18). W. D., male, aged forty-nine, entered the hospital because of diarrhea and cramps of six months' duration. His first symptoms had occurred six months before admission with an attack of diarrhea, cramps and malaise lasting about three days. There were four to five loose stools daily. Several months later the same symptoms recurred and had been present ever since with copious, watery, foul stools which were brown in color. There was a 50 pound weight loss. A month before admission, swelling of the ankles occurred, associated with extreme weakness.

Physically, the patient showed considerable emaciation. His blood pressure was 100/74. There was arteriosclerosis and the fingers and toes were clubbed and cyanosis of the nail beds was present.

Fig. 17. Case xi. The small intestinal pattern following a barium meal is definitely abnormal. It shows clumping and dilatation and a loss of the feathery appearance indicating the so-called dietary deficiency pattern.

Fig. 18. Case xi. The periosteal proliferation is best seen involving the fibula.

A roentgenogram of the chest at the time of admission was reported as negative. Roentgenograms of the extremities showed slight demineralization of the femora and humeri. There was no periosteal proliferation at this time. Barium enema was negative. A gastrointestinal series showed a normal esophagus, stomach and duodenum. The small intestinal pattern was definitely abnormal. It showed the clumping, dilatation and loss of valvulae conniventes, described as the dietary deficiency pattern. After a month of intensive therapy consisting of a high caloric, low fat diet with folic acid, heavy doses of vitamin A and D and calcium lactate, the patient showed clinical improvement. Re-examination of the small intestine showed an improved pattern. However, roentgenograms of the extremities revealed extensive hypertrophic osteoarthropathy of the femora, tibiae and fibulae with demineralization. The upper extremities and feet showed similar changes. The chest roentgenogram was still reported as negative. About six weeks later, re-study of the extremities presented evidence of periosteal proliferation involving the femora,

tibiae and fibulae. Improvement had occurred in the other bones and these were reported as normal. This corresponded to the clinical improvement of the patient, although a small intestinal study still showed some abnormality of the intestines.

Stool cultures were consistently reported as negative throughout the entire illness. The blood count showed no abnormality except for a moderate anemia. Gastric analysis showed no free hydrochloric acid.

The patient was discharged in an improved condition with a diagnosis of non-tropical sprue. He is still being followed in the clinic and apparently further improvement is gradually occurring.

DISCUSSION

The presence of joint symptoms in previously healthy individuals should be carefully evaluated in order to determine the possibility of a co-existing underlying pathological condition. In 8 of these cases an associated disease was present which first manifested itself by painful or swollen joints. Roentgenographic examination of the joints led to the discovery of periosteal new bone formation with subsequent investigation establishing the proper diagnosis. Six of these cases were definitely proved cancers of the lungs, the most common being bronchogenic carcinoma. In 2 other cases, the diagnosis was almost certainly a lung malignancy but positive pathological proof could not be obtained. Case VIII was undiagnosed, but the roentgenogram showed pulmonary abnormality. In only 2 of our series was the primary disease outside of the respiratory tract. One of these was a chronic myelogenous leukemia with generalized adenopathy. It is quite possible that the mediastinal nodes could have been involved. The other was a case of non-tropical sprue. In practically all the cases of this series, an improvement in the primary disease was associated with an improvement in the symptomatology secondary to the hypertropuic pulmonary osteoarthropathy.

SUMMARY AND CONCLUSION

1. Symptoms of joint pain and swelling simulating arthritis may be due to hypertrophic pulmonary osteoarthrophy.

2. Roentgenologic demonstrations of periosteal new bone formation should lead to further investigation of the underlying primary disease.

3. The most common site of the primary disease is within the pulmonary tract, although other systems may be involved. The most common condition is malignant growth of the lung.

4. The etiology of hypertrophic pulmonary osteoarthropathy has not as yet been definitely determined.

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SCLEROSIS OF BONES IN GAUCHER'S DISEASE*

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BONE changes in Gaucher's disease are generally considered as destructive lesions. Their progress is slow. Their roentgenological appearance is characterized by mottling and rarefaction of bone structures and expansion and deformity of the bones involved. The cortex of long bones may become thinner because of erosion of the inner layers induced by proliferating Gaucher cells. Absorption from the inside and accretion on the outside produce the characteristic club-shaped or fusiform widening "Erlenmeyer flask" deformity of the shaft of the femur. Further abnormalities are changes of shape and structure of the head of the femur with softening of the neck, collapse of vertebral bodies with gibbus, pathological fractures, and others.

While roentgen signs of these abnormalities and their patho-anatomical fundamentals have often been discussed, very little attention has been directed toward proliferative bone changes. Although several investigators maintain that mottled areas of bone erosions may alternate with condensation,[1,2,3,5,7] and bone destruction may be intermingled with areas of sclerosis, on the whole, pathological ossification has not been considered as an integral feature of osseous manifestations of the disease.

We had the opportunity to study bone changes in 2 cases of Gaucher's disease and

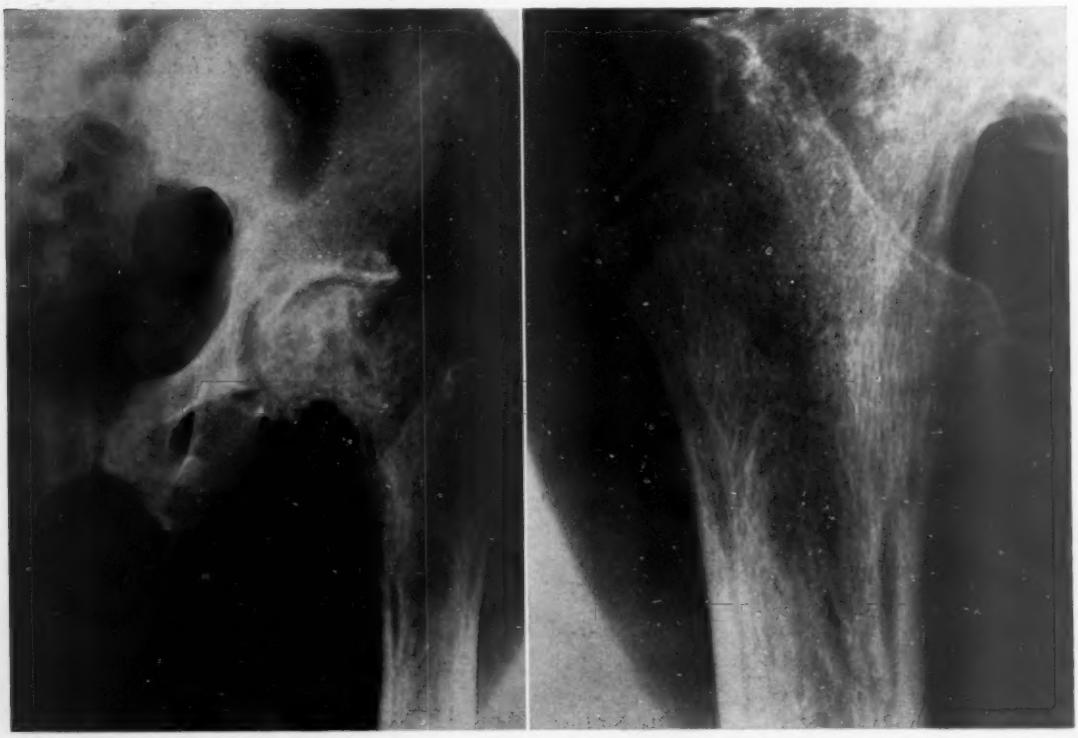

FIG. 1. The patient (No. 31799) was a male, aged fifty-two, with Gaucher's splenomegaly. Roentgenograms show deformity of the head of the left femur with translucent areas surrounded by densities. Bone cylinder in medullary cavity seen below trochanters.

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found that in both more or less marked new formation of bone tissue was recognizable. A third case that came to our attention also showed similar findings.

Our first patient was under observation for twenty-four years. The first beginnings of bone changes were hypertrophic fringes around the left acetabulum and faint mottlings of the structure of the head with signs of condensation. The case was interpreted during the first seven years as being a low grade infectious arthritis with regenerative bone changes. Later bone tissue was laid down in the intertrochanteric area, and finally a hollow bone cylinder developed inside the medullary cavity, running parallel to the cortex from the trochanters to the middle of the shaft of the femur, occupying the peripheral portions of the marrow (Fig. 1). In the distal portions of the femur diffuse bone formation prevailed intermingled with faint translucent areas (Fig. 2). The case was verified at a laparotomy made for removal of gallstones.

Similar "bone cylinders" were seen in the marrow cavity of both femora in another instance of the disease occurring in a young soldier. The roentgenograms of this case were presented at the San Francisco

Fig. 2. Same patient as in Figure 1, showing diffuse bone formation in medullary cavity of the lower left femur.

Fig. 3. The patient (No. 239849) was an Indian boy, aged two, with splenomegaly. *A*, normal appearing left femur in Gaucher's disease. *B*, same femur eight months after splenectomy revealing thickening of the cortex with signs of faint diffuse bone formation in the medullary cavity.

X-Ray Study Club in 1944. They revealed fusiform expansion of the distal half of both femora. Bands of ossification were seen running parallel to the cortex in the medullary space. They had the width of approximately 5 mm. on each side and were separated from the inner aspects of the cortex by a space, measuring approximately 1 or 2 mm. They extended almost the length of the femur. The disease was verified histopathologically after splenectomy. Further data on this patient are not at hand.

In our second case, the disease was observed in two year old Indian boy. The first roentgen survey showed a normal skeleton. Both femora revealed no abnormal findings (Fig. 3*A*). Eight months later, however, following surgical removal of the

Fig. 4, *A* and *B*. The patient (No. 239549) was a female, aged fifty-six. Roentgenograms show pathological fracture of the neck of the left femur with numerous translucencies about the fracture and in the intertrochanteric area. Absence of bone sclerosis makes Gaucher's disease unlikely, despite Erlenmeyer flask deformity of shaft of femur. Autopsy diagnosis: hemocytoblastic myeloma.

enlarged spleen, thickening of the cortex of the right femur and signs of faint pathological ossifications were exhibited in distal portions of the marrow cavity (Fig. 3*B*). We explained this remarkable event by assuming that proliferations of Gaucher's structures were already present in the marrow prior to splenectomy. At that time they produced no roentgen signs. Appearance of ossifications eight months after removal of the spleen indicated that in the meantime the Gaucher proliferations had undergone retrogressive changes which were associated with bone formation.

The process of osteogenesis in Gaucher's disease was first described by Pick. He found that the argentophile reticulum produced by cells of reticulo-endothelial hyperplasias becomes transformed into collagenous structures, while the specific cells themselves gradually disappear. They are replaced by dense, sclerotic connective tissue. Bone formation takes place as a direct metaplasia of connective fibers and not by osteoblastic activity. Consequently newly formed bone spicules are not the products of the osteogenic mesenchyma. Similar observations were made by us[11] in leukemic forms of reticulo-endothelioses (monocytic leukemia).

It seems that ossifications in the bone marrow in cases of Gaucher's disease are not incidental findings. They are tissue products of reticulo-endothelial proliferations developing as direct osseous metaplasias of reticular and collagenous fibers. These in turn are contributed by the reticular cells themselves, mainly as replacements of degenerating and aged cells.

Despite the fact that no attention has been paid until now to sclerotic changes in Gaucher's disease, sclerosis of bones is recognizable on roentgenograms illustrating several articles (ref. 4, Fig. 3 and 8), (ref. 5, Fig. 5), (ref. 6, Fig. 1), (ref. 9, Fig. 6), (ref. 10, Fig. 4), and others. It is conceivable that no signs of pathological bone formation will be exhibited in early skeletal manifestations of Gaucher's disease. In such cases probably only the absorptive or destructive phases of bone changes are manifest, and the productive phase is held in abeyance. The late appearance of bone formation in spongy structures adjacent to bone erosions may be misinterpreted as signs of reactions of osseous regenerations in the vicinity of inflammatory lesions. This is probably the reason why the similarity of bones in Gaucher's disease to those of osteomyelitis and chronic tuberculosis is not infrequently recorded.[8]

In our second case pathological ossification in the bone marrow became visible in a child as soon as eight months after splenectomy. In connection with the above considerations we have to assume that removal of the spleen influenced the vitality of Gaucher cells in the bone marrow. It probably caused retrogressive changes which were associated with development of fibrous structures. These in turn formed the ossifications seen on the roentgenograms. Although splenectomy is no "cure" in Gaucher's disease, the consensus is that removal of the spleen usually improves the clinical condition of the patient. This is due not only to physical factors but also to immediate improvement of blood formation, sudden increase of platelets in the peripheral blood, decrease of bleeding time, and so forth, as was observed in our case also.

Recently we had the opportunity to see the Erlenmeyer flask deformity in the middle and distal portions of the right femur in the case of a woman, aged fifty-six. We considered this sign to be indicative of Gaucher's disease. The patient had been suffering for several months from a pathological fracture of the neck of the femur. The bone structure was mottled in the surroundings of the fracture and also in the head and in the intertrochanteric areas. No signs of bone formation were exhibited however, in structures adjoining the mottled areas of the femur or in the marrow cavity of the expanded shaft during the one and one-half years of observation. Autopsy revealed that bone changes were caused not by Gaucher's disease but by the rare disorder of hemocytoblastic myeloma (Fig. 4, *A*, *B*).

Absence of ossification in this case, in which all other roentgen signs were characteristic of Gaucher's disease corroborates our belief that ossifications in the medullary cavity and in spongy structures are integral findings in advanced cases of this disorder.

SUMMARY

Attention is called to the frequent presence of roentgenological signs of bone formation in the medullary cavity in cases of Gaucher's disease. The new formation of osseous tissue is not excessive and is similar in appearance to regenerative ossification in the surroundings of inflammatory lesions. They occur, however, not only in bone structures adjoining absorptive changes but also in such parts of the medullary cavity in which no roentgenological signs of bone destruction are exhibited. In two of our observations bone cylinders were present and occupied the peripheral portions of the medullary cavity in the proximal two-thirds of the femur.

Bone tissue is laid down in such cases in intercellular fibrous structures of Gaucher proliferations as a product of direct metaplasia of collagenous fibers. Such fibers are in abundance in late stages of the disease. Consequently, the presence of ossifications in the medullary cavity or in spongy areas indicates localized or general ageing of the pathological tissues. In early manifestations no appreciable amount of fibers is formed. Therefore, pathological osteogenesis may be absent.

Roentgen signs of pathological ossification in Gaucher's disease may be of diagnostic significance. This occurs if newly formed bone tissue is laid down in areas situated about absorptive lesions and involves simultaneously more remote areas of the medullary cavity in which no destructive changes are evident.

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Vol. 60, No. 2

A CASE OF LONG STANDING SICKLE CELL ANEMIA WITH MARKED BONE CHANGES*

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SICKLE cell anemia can be classified among the chronic hemolytic anemias. It is a hereditary disease first described by Herrick[3] in 1910 and exclusively limited to persons of Negro ancestry. It is important to distinguish between individuals suffering from "sickle cell anemia" and those just bearing the "sickle trait." The latter is a dominant asymptomatic finding in about 5 to 10 per cent of American or West African Negroes. Person afflicted with sickle cell anemia usually do not live beyond the age of thirty. They die in early life from intercurrent infection, vascular thrombosis or uremia, thus limiting the propagation of the disease.

CLINICAL PICTURE

Sickle cell anemia is characterized by attacks of excessive blood destruction resulting in anemia, pallor, icterus, weakness, shortness of breath, joint and abdominal pains, splenomegaly, hepatomegaly, chronic leg ulcers, and gallstones. Between attacks there may be few or no symptoms. The increased demand upon the hematopoietic system results in increased medullary activity. This hyperactivity of the bone marrow produces the characteristic roentgenographic skeletal changes.

ROENTGEN FINDINGS

Few papers have appeared dealing with the roentgen findings occurring in sickle cell anemia since the excellent review by Caffey[1] in 1937. He pointed out that the appearance time of the first detectable roentgen changes following the clinical appearance of the disease varies considerably. In 1941 Danford, Marr and Elsey,[2] described a case of sickle cell anemia in an eight month old Negro infant who already presented roentgen evidence of bone changes. The lesions were stated to have disappeared after repeated blood transfusions and generally improved health of the infant.

CASE REPORT

The patient is a female, married, aged forty-three, referred by Dr. Barrett to the Salt Lake County General Hospital with the diagnosis of "sickle cell anemia."

Past History. She stated that she had had joint pains in her arms and legs throughout her life. Splenomegaly was observed when she was three years old and has been present off and on ever since. Her teeth did not erupt until she was nine years old and when they finally appeared they were crooked, malformed and had to be extracted. A plastic repair was done on the gums. During the past ten years she has been suffering from chronic recurrent leg ulcers, increasing deafness and monthly episodes of epistaxis independent of the menstrual cycle. There is a history of irregular menstruation with no real cycles. The bleeding lasts from one to three weeks and is quite profuse without dysmenorrhea. There has never been any purpura. Attacks of generalized abdominal pain have occurred since the age of sixteen.

She has never been pregnant though no contraceptives have ever been used. In 1943, a bilateral salpingectomy (endosalpingitis), removal of ovarian cyst, uterine suspension and appendectomy were performed at another hospital.

Rheumatic heart disease was diagnosed at the age of nine and digitalis taken intermit-

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tently since then. During the past few years she has developed mild pitting edema of ankles. Weakness, tiredness and anorexia have been prominent as long as she can remember. In spite of this she has been doing housework and working as a sales clerk. Several years ago she was told that she was suffering from an anemia "which probably came from her Negro grandfather."

Family History. Her father is half Indian and half white. He died of "dropsy" at the age of forty-five. Her mother is half Mexican and half Negro, aged seventy and well. Five siblings are living and well. There are no other known cases of sickle cell anemia in the family.

Physical Examination. The patient is a slender, chronically ill looking woman who bears many negroid facial features. The physical examination is not remarkable except for the following: There is bilateral middle ear deafness. The drums are normal.

Heart: The point of maximal impulse is 12 cm. from the mid-sternal line in the fifth left intercostal space. The right heart border is 3 cm. from the midsternal line in the fifth intercostal space. The rhythm is regular, the rate 80. A rough systolic murmur is heard over the apex.

Abdomen: There is an old, well healed midline incisional scar. The liver can be palpated 4 cm. below the costal margin. Rectopelvic findings suggest uterine myomas.

Extremities: There is shallow, clean granulating ulcer measuring 4 by 5 cm. on the medial aspect of the lower right leg and evidence of old scars on the left leg.

Laboratory Data (see Table 1).

Blood smear: Anisocytosis, poikilocytosis and basophilic stippling 1 to 3 plus. Hypochromasia—1 plus. Twenty to 31 nucleated red cells.

Table I

LABORATORY DATA

	Normal	October 21, 1946	November 7, 1946
Leukocyte count	5–10,000	15,000	23,000
Juveniles	3–5%	1%	10%
Polymorphonuclears	54–62%	57%	62%
Eosinophiles	1–3%	4%	4%
Lymphocytes	25–33%	28%	18%
Monocytes	3–7%	10%	6%
Red blood cell count	4.2–5.4 million	3.4 million	2.09 million
Hemoglobin	12–16 gm.	8 gm.	5 gm.
Hematocrit	34–47	23	15
Mean corpuscular volume	82–92	67	71
Mean corpuscular hemoglobin	27.31	22	24
Mean corpuscular hemoglobin concentration	32–36	34	33
Reticulocytes	0.5–2%	15%	13%
Icteric index	4–6	30	75
Erythrocyte sedimentation rate	0–15	3	67 uncorrected
Bleeding time	1–5 min.	2 min.	1 min.
Clotting time	2–5 min.	3 min.	
Clot. retr.	2–3 hr.	1 hr.	1 hr.
B.U.N.	8–15 mg. per 100 cc.	21	23
Calcium	9–11 mg. per 100 cc.	11.4	
Phosphorus	3–4 mg. per 100 cc.	4.2	
Kahn test		Negative	
Fragility test	.30–.36% NaCl	.18% NaCl	

Fresh preparation shows 95 per cent sickling.

Van den Bergh test:

One minute (direct 1.08 mg.)
(normal 0–.25 mg.)

Thirty minutes (total 1.22 mg.)
(normal to 1.2 mg.)

Stool: 9,000 Ehrlich units urobilinogen. Guaiac test negative.

Gastric analysis: No free acid after histamine. Urine urobilinogen normal.

Electrocardiogram. Normal.

Roentgen Findings.

Posteroanterior roentgenogram of the chest: The lung fields are clear. The transverse diameter of the cardiac silhouette is at the upper limits of normal. There is a calcific plaque in the knob of the aorta.

Skull roentgenograms (anteroposterior, lateral (Fig. 1) and basal views): The findings here are very unusual in that the bones of the vault are extremely thick. It is impossible to delineate the tables because of the increased density of the calvarium. The frontal sinuses are large and well aerated. The mastoids in contradistinction show an almost complete lack of pneumatization. There is an irregular defect in the left parietal bone measuring 1.5 by 2 cm. This has a sclerotic margin.

Fig. 1. Skull (lateral view). There is absence of delineation of the tables. The bones are dense and and sclerotic. The mastoids have failed to pneumatize.

Posteroanterior roentgenogram of both hands: There is almost complete loss of the trabecular pattern of the shafts of the metacarpals and phalanges. The cortex is markedly thickened. The second phalanx of the middle finger and the fifth metacarpal bone of the right hand show cyst-like areas within the medullary cavity with expansion of the shafts.

Extremities (Fig. 2 and 3): Both fibulae and ulnar bones show cortical thickening. In some areas there is widening and increased trabeculation of the medullary cavity with concomitant thinning of the adjacent cortex. There is marked variation in density suggesting cyst formation. The upper third of the left tibia shows marked overgrowth of the cortical bone so that it encroaches upon the medullary cavity.

Roentgenogram of right upper quadrant (Fig. 4). There are numerous facetted and laminated calculi outlining the gallbladder. There is a solitary stone at the level of the first lumbar intervertebral disc which may be in the cystic duct.

DISCUSSION

This case shows many of the typical features of sickle cell anemia. There is a history of splenomegaly intermittently for forty years. The liver is at present enlarged. Rheumatic heart disease was diagnosed at one time because of the migrating joint pains, the abdominal pains, the heart murmur and the leukocytosis. This is a frequent diagnostic error. Many of these cases are

Fig. 2. Lower extremity (lateral view). There is localized thickening of the cortex of the upper third of the shaft of the tibia. This appears to encroach upon the medullary cavity.

also mistakenly diagnosed as acute abdominal emergencies and operated on. The diagnosis can be made by examining a wet blood smear preparation for evidence of sickling. When dealing with the "sickle trait," sickling may not appear for six to twenty-four hours, whereas in sickle cell anemia it shows up in thirty minutes to a few hours.

Chronic leg ulcers, gallstones and epistaxis as seen here are frequent in persons

Fig. 3. Forearm (lateral view). There is irregular thickening of the cortex. The architectural pattern shows some increase in trabeculation.

suffering from sickle cell anemia as well as other chronic hemolytic anemias.

The bone changes that develop apparently depend on the degree of strain placed on the hematopoietic reservoir. That is why they are probably rarely described in young children. Most authors agree that the skull changes are similar to but less pronounced than those observed in erythroblastic anemia. They usually find widening of the tables of the vault associated with vertical striations. Thickening of the diploe results with loss of definition of the outer table.

Changes in the long bones seem to be less frequent. Usually the cortex is thickened as opposed to thalassemia in which it is thinned. Osteosclerosis and new bone formation within the medullary cavity

Fig. 4. Right upper quadrant. There are numerous facetted and laminated calculi outlining the gallbladder.

have been reported. At times this is associated with scattered translucent areas.

The combined cortical thinning and thickening such as seen in the case reported here have not been noted in other cases. The involvement of the whole calvarium including the mastoids by an osteosclerotic

process rather than the "hair on end" striations is unusual. Previous publications do not mention the increased reticulation in the flat and short bones nor the cystic areas noted in the tubular bones of the hand such as are present in this case.

SUMMARY

A case of long standing sickle cell anemia is described, showing unusual roentgen changes in the skull, tubular and flat bones.

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DIVERTICULOSIS OF THE GALLBLADDER

CASE REPORT

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SINCE Bársony's original report of a single diverticulum of the gallbladder, confirmed by operation, similar cases have been sporadically recorded in the literature by other writers. The roentgenologic features of these diverticula have also been described by Vastine, Paillard and Paillard, and by Hartmann. Diverticulosis of the gallbladder seems to escape roentgenologic detection completely and, according to Weisel and Walters, is almost exclusively recognized at operation or on pathological examination.

Recently we had the opportunity to observe a patient with cholelithiasis associated with diverticulosis of the viscus, demonstrated by cholecystography. It may therefore be justified to report this case and to present a brief discussion of the subject.

The problem of pathogenesis of gallbladder diverticula, and, more particularly, their relation to other diseases of the gallbladder has been the subject of extensive clinical and pathological studies. Rokitansky, who first described hernia-like outpouchings of the gallbladder mucosa, noted that they frequently contained small stones completely separated from the lumen of the viscus. Aschoff was convinced that diverticula, which he confused with Luschka's ducts, played an important role in the pathogenesis of cholecystitis and cholelithiasis, with which they are commonly associated. He suggested that prolonged stasis and increased intracystic pressure within a diseased gallbladder caused a gradual increase in size of small crypts, encountered also in the walls of normal gallbladders, until they penetrated through the muscular coat and formed "false diverticula." These invaginations occurred usually along the path of vessels passing between muscle bundles of the vesical wall and often were the seat of small stones.

Halpert concurred with Aschoff that diverticula were more common in the presence of gallbladder disease, but was emphatic in drawing a distinction between these structures and "true Luschka's ducts," which he defined as aberrant bile ducts in no way related to diverticula. This author preferred to designate the latter as "Rokitansky-Aschoff sinuses," and stated that their development depended: (1) on the relative strength and development of individual muscle bundles and their relation to each other; (2) on the number and size of the blood vessels passing through the intermuscular spaces and their mode of penetration; and (3) on the state of contraction of the gallbladder and any condition, especially pathologic, which influenced its contractibility.

Experimental studies by Higgins, and Higgins and Mann, disclosed that, in guinea pigs, contractions of the gallbladder wall were rather isolated, independent and accompanied by formation of small herniations; no rhythmic peristaltic waves were observed. In 1923 Westphal demonstrated that neurogenic disturbances, causing a spasm of the sphincter at the terminal portion of the common duct simultaneously with strong contractions of the vesical wall, were capable of producing multiple diverticula. Clinical observations confirmed the existence of a similar symptom complex in man; the symptoms consist of biliary colics in the absence of cholecystitis or cholelithiasis and are now generally attributed to dyskinesia of the gallbladder, particularly when irregular contractions of the latter are demonstrated by cholecystography.

The high incidence of diverticula in indi-

viduals suffering from cholecystitis or cholelithiasis has been generally emphasized. Robertson and Ferguson reviewed this subject recently, and presented the results of their own investigation of 495 gallbladders, comprising 175 postmortem and 320 surgical specimens. They classified diverticula into three grades, depending on the depth of penetration of the vesical wall. In the first grade the crypts extended to the muscular coat; in the second grade the invaginations penetrated into the intermuscular lacunae, and in the third grade, the diverticula penetrated through the muscular wall into the underlying connective tissues, occasionally reaching the serosa. Normal gallbladders of this series contained few superficial diverticula. Gallbladders evidencing previous inflammation without gallstones showed diverticula classified as Grade 2 in approximately 70 per cent of the examined specimen. Occasionally these were partially or completely cut off from the lumen of the bladder and dilated into cysts. In some cases, typical gallstones lay within the closed off crypts, while in others, calculi could be expressed into the lumen through the communicating "ducts." All degrees of inflammation leading to abscess formation, complete obliteration of the epithelial cells normally lining the spaces, and even rupture into the periotoneal cavity or the liver, were also observed. There was no definite indication that gallstones contributed significantly to the frequency or number of demonstrable diverticula.

Robertson and Ferguson were in agreement with previous writers, who saw a similarity between diverticula of the gallbladder and those encountered in the intestinal tract and in the urinary bladder. The fact that diverticula of the gallbladder were more frequent and numerous in the older age group suggested to them that invagination of the mucosa followed abnormal pressures, exerted during stages of abnormal contractions or relaxations of the underlying muscle bundles of a constitutionally "weak" viscus. They, too, emphasized the significance of neurogenic dysfunctional states of the extrahepatic biliary system in the pathogenesis of diverticula, though they did not deny the possible significance of stones and chronic inflammation as an additional etiologic factor, chiefly due to obstruction and increased intracystic pressure.

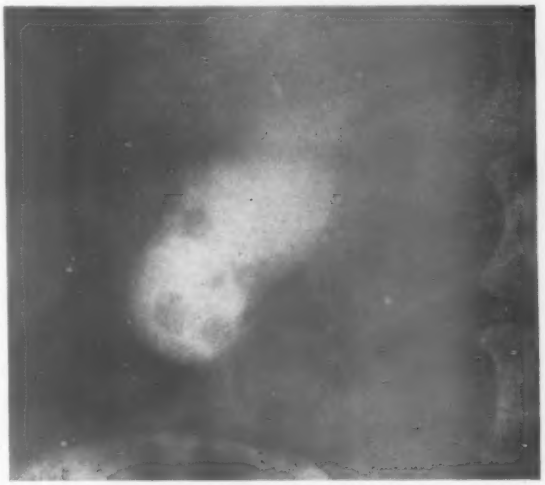

Fig. 1. Small sessile densities along the lateral wall of the gallbladder.

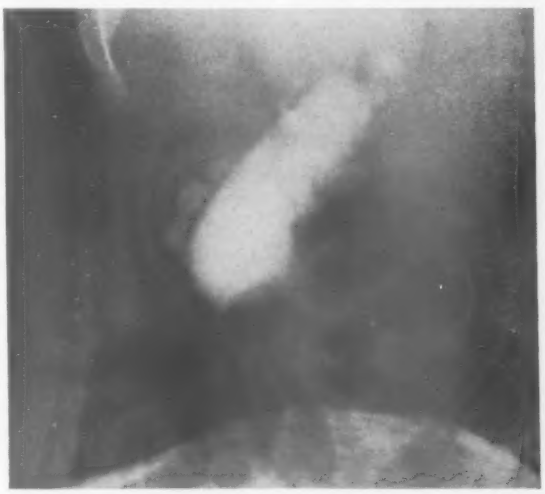

Fig. 2. The diverticula are clearly demonstrated after ingestion of fatty meal.

CASE REPORT

A middle aged, white female complained for several years of pain in the epigastrium, ag-

Fig. 3. Non-opaque stone near the neck of the gallbladder.

gravated by food containing fat. The symptoms were not severe and were usually relieved by an adequate diet. There was no history of colic or jaundice. The stools were not discolored. The patient was not hospitalized, but a routine roentgen examination of the gallbladder was made as a part of a medical examination.

The cholecystograms revealed a well visualized gallbladder, of normal size and in normal position. There were numerous diverticula arising from the walls of the gallbladder, which protruded beyond the outline of the viscus. Short "ducts" connected the diverticula with the bladder wall. One non-opaque stone was present within the lumen of the gallbladder. There was good contraction of the organ and concentration of the dye after fatty meal. A diagnosis of cholelithiasis and diverticulosis was made and cholecystectomy was advised.

COMMENT

Although, pathologically, diverticulosis has been shown to occur frequently in diseased gallbladders, it is seldom demonstrated roentgenologically. This is not surprising if one considers that the small ducts, through which diverticula communicate with the lumen of the bladder, are often occluded, preventing the dye from entering the diverticula. Small stones within the diverticula may also prevent an adequate visualization, even if the gallbladder itself should be demonstrated. These stones, when opaque, may be erroneously interpreted, because they appear to lie outside the visualized organ and do not seem to be related to it.

The roentgenologic characteristics of diverticula are essentially similar to those in the intestinal tract or the urinary bladder. The size of these structures in our case was comparable with diverticula frequently seen in the colon.

It appears rather obvious that diverticulosis of the gallbladder can be demonstrated roentgenologically when the conditions for visualization of mucosal invaginations are favorable, i.e., when the communicating ducts are patent and there are no stones within the diverticula. An inflammatory process of the gallbladder, accompanied by edema and occlusion of the lumina of these "ducts," will in most instances prevent their recognition.

The possibility of diverticulosis should be considered in the presence of small, irregularly distributed opacities in the region of the gallbladder, particularly when the clinical history suggests disease of the biliary tract, and the distribution of these opacities is such that it corresponds with the anatomical contour of the gallbladder.

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DEPARTMENT OF TECHNIQUE

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A MONITOR METER*

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THE following is a description of a simple monitor meter which is permanently built into a roentgen therapy tube stand for the purpose of giving a continuous check on the output, thereby giving the operator as indication of any change in the expected output which may have taken place as the result of a wrong filter, wrong voltage or amperage setting, slippage of the tube within the housing, or for any other reason.

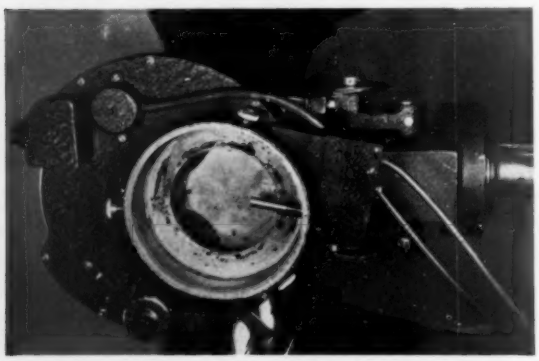

FIG. 1. Ionization chamber mounted in Westinghouse therapy tube stand.

The principal feature of this instrument is that it employs a small ionization chamber which is placed on the edge of the field and therefore does not cast any shadow on that portion of the field normally used for therapy, and causes no increased filtration to the beam, but most important of all, as the space which it occupies is so small, it does not interfere with the machine being operated very close to the patient. There is no interference with any cones.

Figure 1 shows the monitor meter mounted in a Westinghouse therapy machine where the thimble chamber is in the beam, and the metal box housing the amplifier and resistors is fastened at some convenient point reasonably close to the chamber.

The chamber is aluminum and of the thinnest walls that can be conveniently machined. Inside dimensions are 7/8 by 3/8 inch. The collector electrode is a piece of No. 18 copper wire, which is insulated by an amber bushing.

Figure 2 shows the above-mentioned equipment as well as the power-pack and milliampere meter. The milliampere meter may be mounted at any desired point on the control stand and the power-pack inside the control stand. An electrolytic condenser should *not* be used.

Figure 3 shows the wiring diagram, which is in no way unconventional except that the positive side of the system is grounded, raising the amplifier tube to a negative potential, which enables the ionization chamber to be at ground potential, thereby simplifying the mechanical construction.

The cable connecting the amplifier to the power supply is two-wire microphone cable with shield and that connecting the

* Presented in the Scientific Exhibit, Forty-eighth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 16–19, 1947.

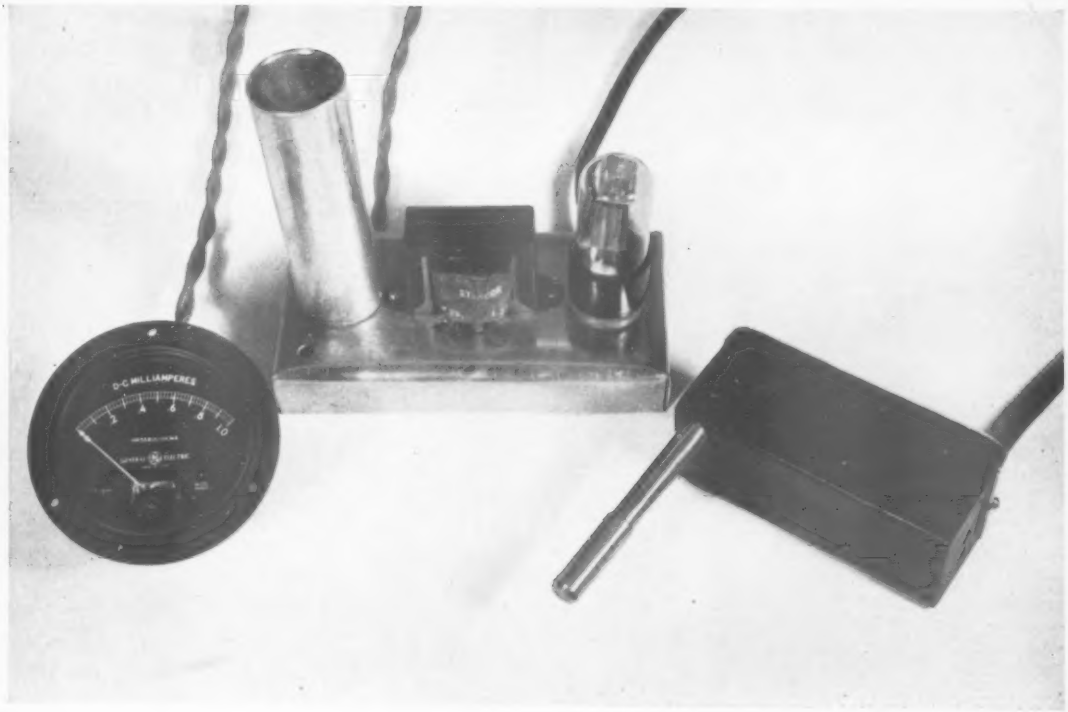

Fig. 2. Component parts of apparatus; amplifier, power-pack, and meter.

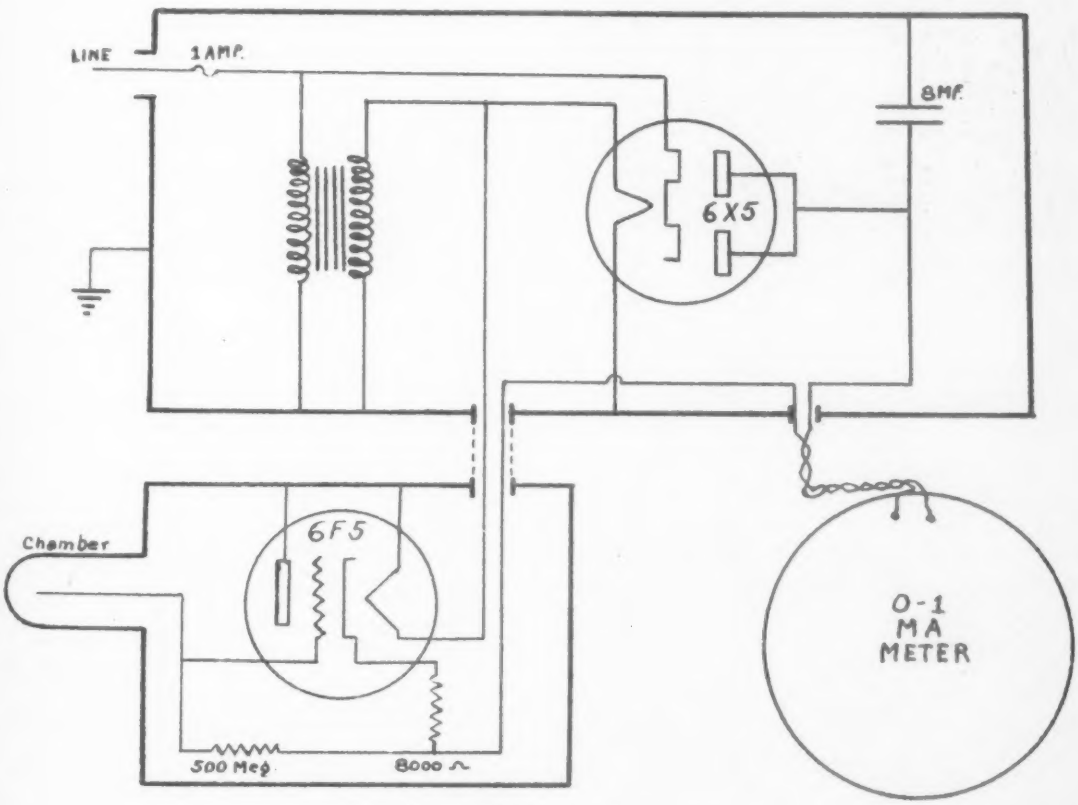

Fig. 3. Wiring diagram.

meter to the power-pack is ordinary twisted lamp cord. These cables may be any desired length.

As fluctuations in line voltage would cause a variance in the reading of this instrument, it is essential that a regulated source of line voltage be used. As most modern therapy machines have a voltage stabilizer in the filament circuit, this instrument may be fed from that source, the required wattage being so low (approximately 9 watts) that no imbalance would result. If no filament stabilizer is available, a small 30 watt line voltage stabilizer, such as built by Raytheon, is now readily available and inexpensive.

To anyone who has not used vacuum tubes of this kind, the following suggestion is made: Obtain several tubes, type 6F5 and, with the meter protected by a resistor of about 1 ohm, leave the instrument in operation for twenty-four hours. After a number of tubes have been aged in this way, the most desirable one will be found.

The sensitivity of the instrument is largely controlled by the cathode resistor which should be a 10 watt wire-wound resistor. It will probably be necessary to try several resistors before such a sensitivity is arrived at to enable full deflection but not to throw the meter off scale.

Normally a well selected tube will give a base current (with no radiation on chamber) of about 0.2 milliampere. No effort is made to buck this out.

The author has used this instrument continuously for approximately ten years and Dr. P. D. Hay of Florence, South Carolina has used one of similar construction for approximately six years, and while it is not intended to be a precision instrument, it has very definitely proved its worth.

103 Rutledge Ave.
Charleston, S. C.

Vol. 60, No. 2

A NEW POSITION FOR CHOLECYSTOGRAPHY

By B. R. KIRKLIN, M.D.
Section on Roentgenology, Mayo Clinic
ROCHESTER, MINNESOTA

ROENTGENOLOGISTS are well aware of certain common handicaps to successful cholecystography and that changes in the roentgenographic position often will overcome them. One of these handicaps is the close proximity of the gallbladder to the spinal column in slender persons, which means that with such a patient in the usual roentgenographic position the shadow of the gallbladder is obscured by that of the spinal column. This can be avoided by directing the rays so obliquely that the shadow of the gallbladder will be projected laterally from that of the spinal column (Fig. 1*a* and *b*). There are also cases in which small gallstones are not demonstrable in the routine posteroanterior view, with the patient prone. In many instances, posteroanterior views with the patient standing will disclose the gallstones in layers (Fig. 2*a*, 2*b*, 3*a* and 3*b*). This technique is so often effective that at one time we considered making it routine in all cases in which a normally functioning gallbladder without visible shadows of stones was depicted, but the idea was abandoned because the success of this technique is so often frustrated by the presence of gas in the bowel.

Gas in loops of intestine overlying the gallbladder is perhaps the most common obstacle to satisfactory cholecystography. For many years we have administered beta-hypophamine (pitressin) hypodermically to eliminate gas whenever it has been found to be present in considerable quantities, and resort to this procedure was deemed necessary in 50 to 60 per cent of patients. Before this agent was employed, the making of new roentgenograms was required for about one-fourth of the patients; whereas in most instances the use of this agent precluded any need of a second examination.

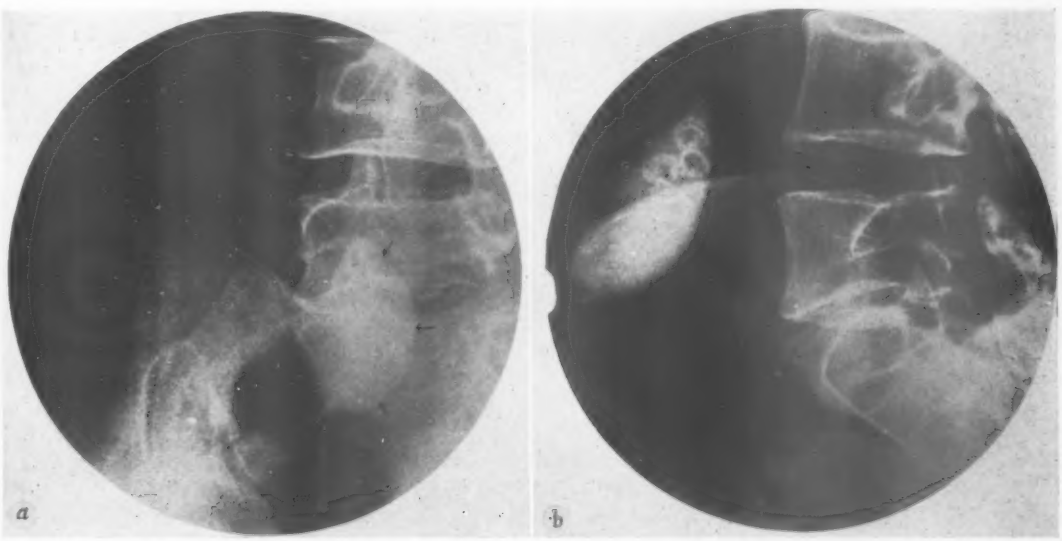

FIG. 1. *a*. Posteroanterior view (patient in the prone position), showing shadow of gallbladder behind that of the lumbar portion of the vertebra and sacrum; *b*, same case, with oblique view separating the shadow of the gallbladder from that of the spinal column and sacrum, and depicting gallstones.

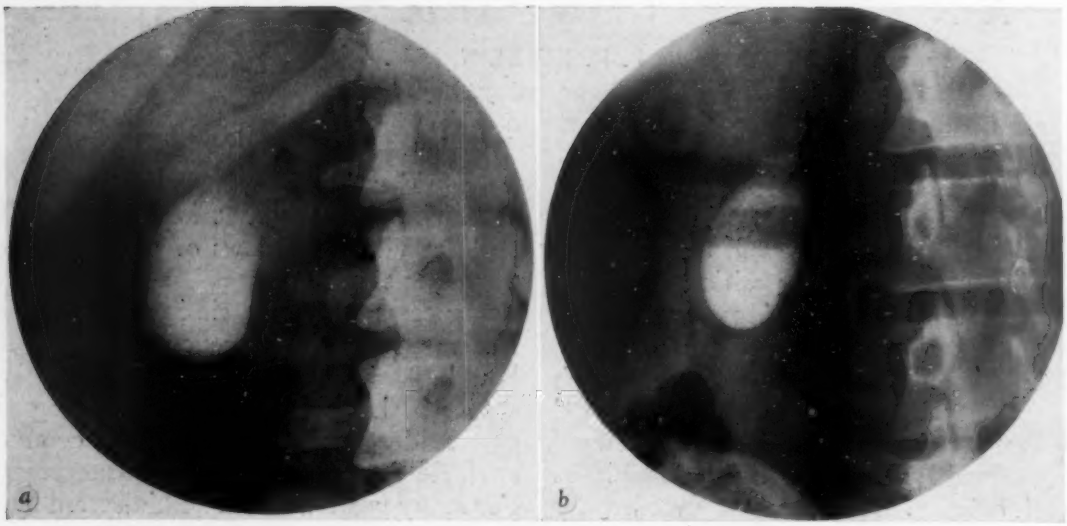

FIG. 2. *a*. A standard posteroanterior view, with the patient in the prone position; *b*, same case, but with the patient standing: note "layering" of gallstones.

Unfortunately, during World War II and shortly thereafter, the exigencies of a wartime economy made pitressin at first difficult to procure and eventually unobtainable, and the problem of overcoming the difficulties caused by intestinal gas again became acute. My chief technician in cholecystography, Mr. Franklin J. Whelan, recalling that changes in the position of the patient and the angle of roentgenography had solved the problem of overlapping shadows of spinal column and gallbladder and of demonstrating layered gallstones, began to try various roentgenographic positions to avoid obscuration of the gallbladder by loops of gas-distended bowel.

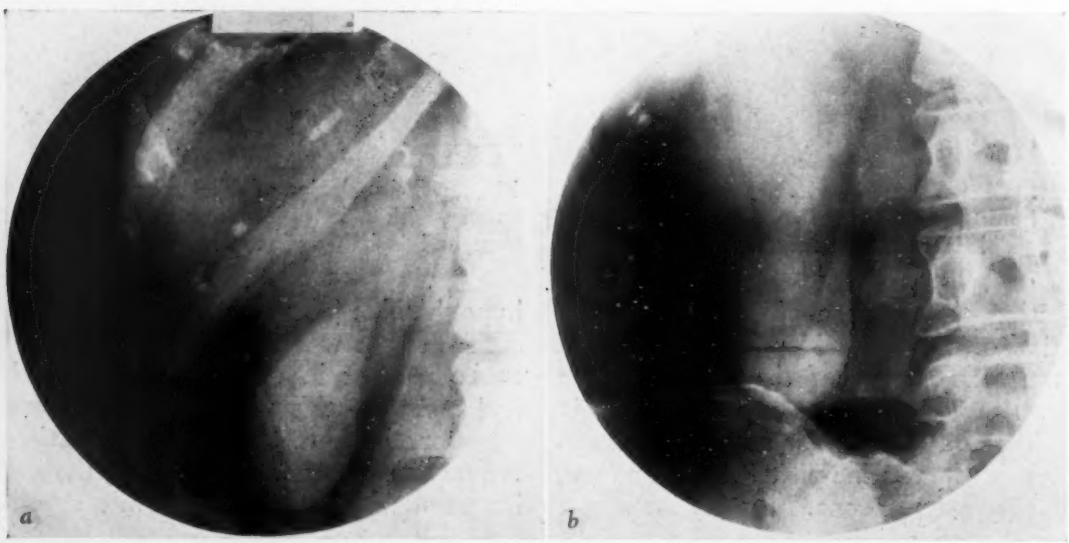

FIG. 3. *a*. Cholecystogram made with the patient in the prone position; *b*, use of the vertical position in the same case, depicting a layer of small gallstones.

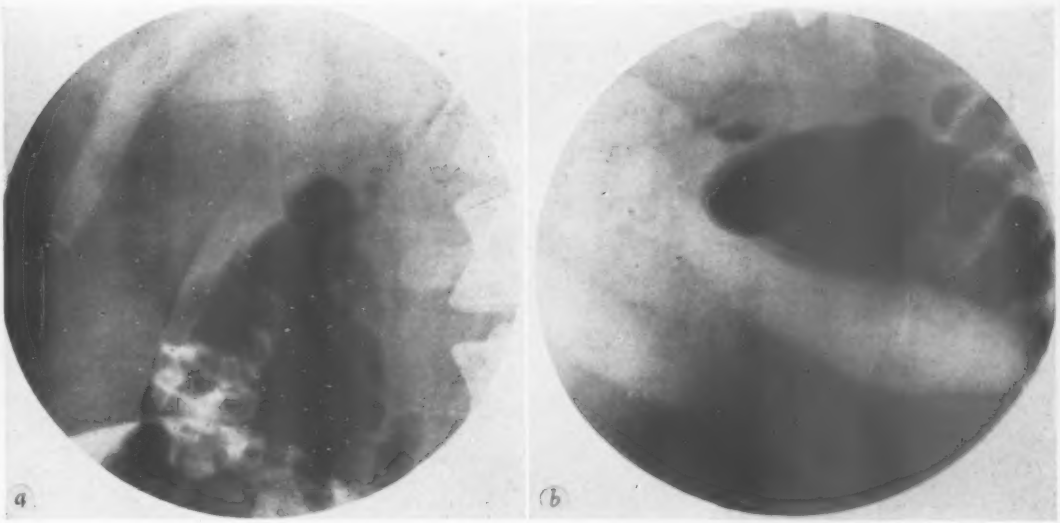

Fig. 4. *a*. Cholecystogram made with the patient in the standard position, showing a normally functioning gallbladder almost obscured by gas in overlying loops of bowel; *b*, posteroanterior view of the gallbladder in the same case, with the patient in the right lateral decubitus position: the gallbladder has fallen away from the gas-distended loops of bowel.

Finally, he decided to employ a posteroanterior view with the patient in right lateral decubitus position. This position permits the gallbladder to gravitate toward the patient's right side and away from loops of bowel in that region. It has all the advantages of the vertical position and is superior to it in that the patient can more easily avoid the movements that blur the shadow of the gallbladder or gallstones, and

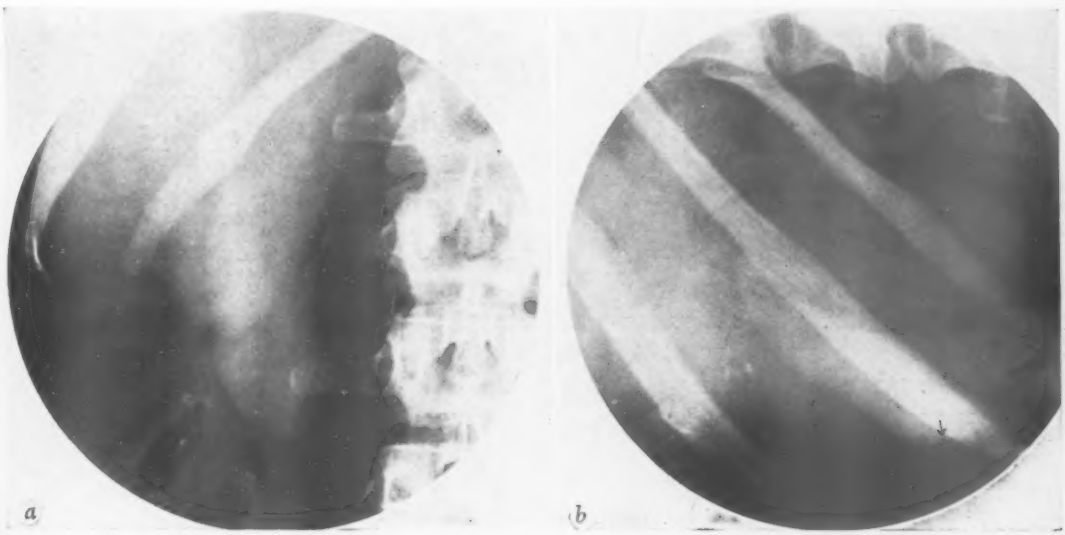

Fig. 5. *a*. Cholecystogram made with the patient in the standard position; it is impossible to identify gallstones; *b*, posteroanterior view in the same case, with the patient in the right lateral decubitus position, showing gallstones lying at the fundus of the gallbladder.

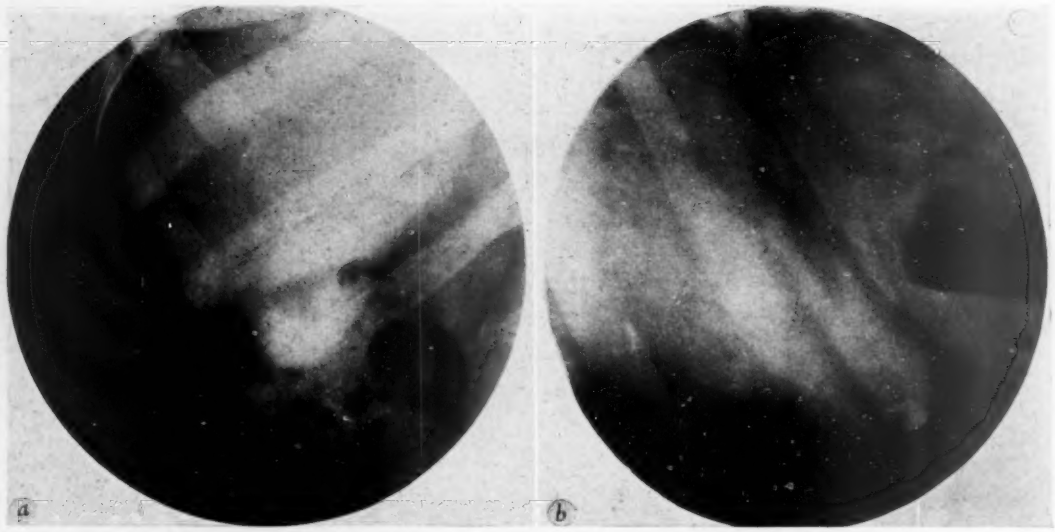

FIG. 6. *a*. Cholecystogram made with the patient in the prone position: the presence of overlying loops of bowel makes it impossible to identify shadows over the fundus of the gallbladder; *b*, posteroanterior view in the same case, with the patient in the right lateral decubitus position: the shadow of the gallbladder and stones is clearly depicted.

it is effective in preventing interference by intestinal gas (Fig. 4*a*, 4*b*, 5*a*, 5*b*, 6*a*, 6*b*, 7*a* and 7*b*). The right lateral decubitus position is also superior for exhibiting the bile ducts, for they will fill with the contrast medium and will be depicted in a greater proportion of cases if this position is used (Fig. 8*a*). Likewise, the position is more

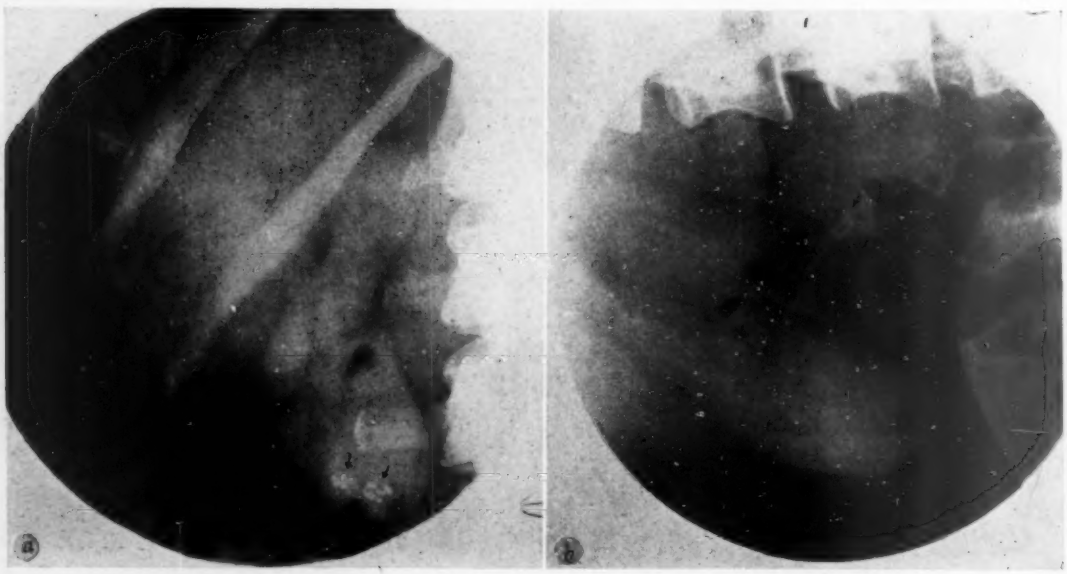

FIG. 7. *a*. Cholecystogram made with the patient in the prone position: note shadows at the fundus of the gallbladder; *b*, posteroanterior view in the same case, with the patient in the right lateral decubitus position: the shadows have not moved with the gallbladder, and therefore are not caused by gallstones.

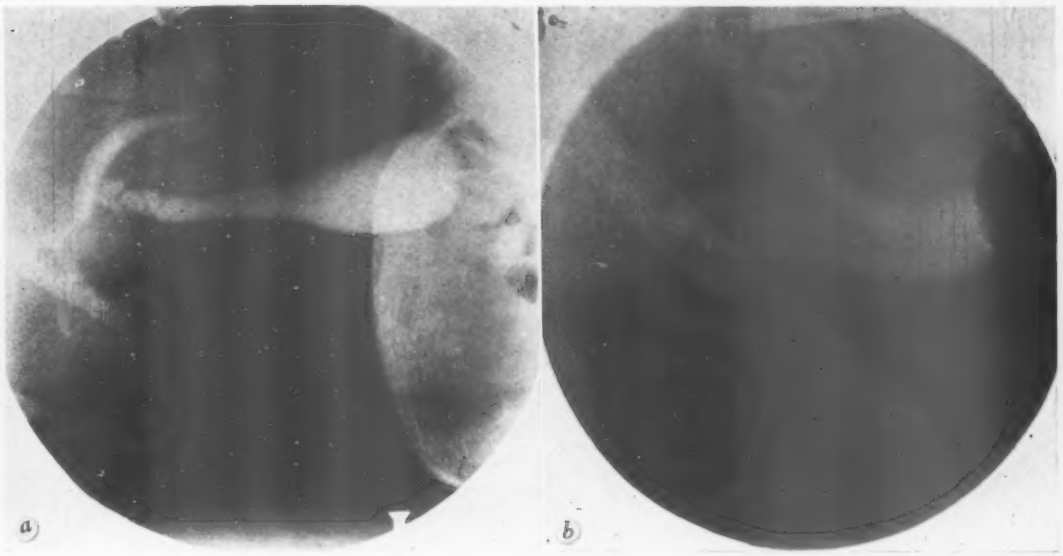

Fig. 8. *a*. Posteroanterior view of the gallbladder with the patient in the right lateral decubitus position, depicting the bile ducts; *b* (not the same patient as in *a*), posteroanterior view of the gallbladder with the patient in the right lateral decubitus position, during the relaxing phase, and showing "layering" of bile.

facile and more effective in demonstrating the layering of the bile that is of academic interest to many examiners (Fig. 8*b*).

The necessary apparatus was improvised by use of a plain high table, a vertical Potter-Bucky diaphragm in conjunction with a cassette changer, such as is used in roentgenography of the thorax, and a standard tube stand. An 8 by 10 inch loaded cassette is attached to the cassette changer, the patient lies in a true right lateral position with his abdomen against the cassette changer; he is immobilized with a canvas band, and the rays are directed horizontally through the area of the gallbladder. A second cholecystogram is made after the second cassette has been attached 2 inches caudad from the first (Fig. 9).

This technique not only averts interference by intestinal gas, but in many cases also exhibits gallstones that are not depicted by other procedures (Fig. 10*a* and *b*). So efficient has the method been that the administration of pitressin, which is now readily available, is not required in more than 1 per cent of our examinations, and consideration is being given to the use of the right lateral posture in all instances

Fig. 9. Right lateral decubitus position of the patient in front of a vertical Potter-Bucky cassette changer to obtain the desired posteroanterior view.

in which the routine prone position reveals a normally functioning gallbladder without evidence of gallstones. However, I do not

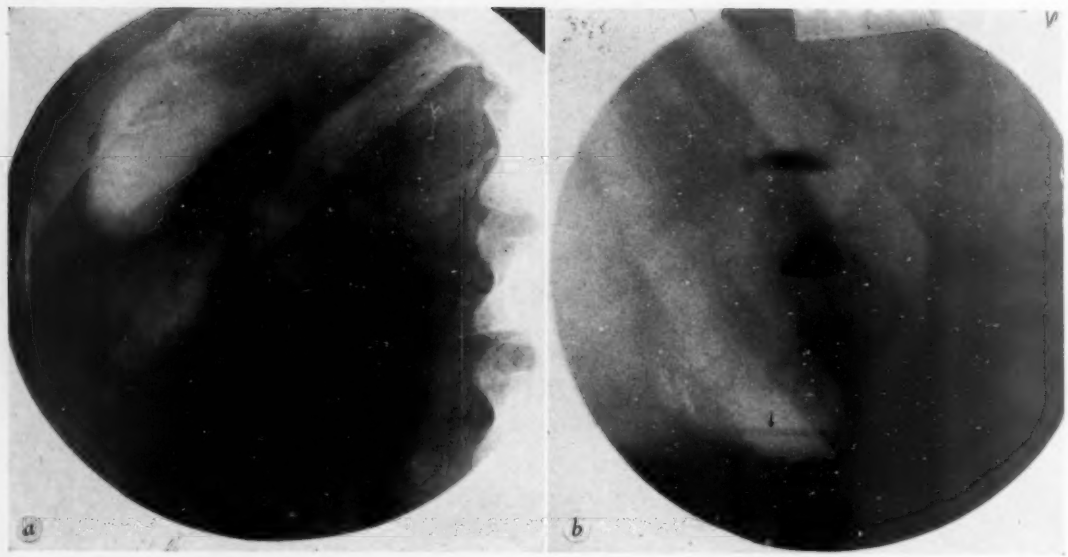

FIG. 10. *a*. Cholecystogram made with the patient in the prone position, showing a normally functioning gallbladder; *b*, posteroanterior view in the same case, with the patient in the right lateral decubitus position, showing a layer of small gallstones.

mean to give the impression that the standard prone position can be discarded, for it is most effective in revealing tumors of the gallbladder, especially adenomas, and should be employed as a routine procedure both before and after administration of the fatty meal.

Section on Roentgenology
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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Thirty-first Annual Meeting: 1949, to be announced.

EDITORIALS

THE RADIOLOGIST CONSIDERS GEIGER COUNTERS

WHILE Geiger counters have been important instruments in the hands of physicists for many years, it is only with the increased availability of radioisotopes that radiologists have become interested in them.

When the radiologist now attempts to read up on this subject and investigate advertisements in the scientific journals, he finds himself rather overwhelmed with the maze of information and technical terms which he has not encountered in clinical work.

The Geiger counter is an extremely sensitive instrument for detecting and possibly measuring many forms of radiant energy and high-speed particles. The essential part of the system consists of an evacuated tube containing an anode and a cathode, the cathode being charged to a high negative potential.

Some tubes require a potential of 800 volts, others as much as 1,500 volts, the voltage for the particular tube being very accurately controlled, because if it is too low, the tube will not operate, and if it is too high, false impulses will be generated.

This tube has in it a small amount of gas at subatmospheric pressure, which, however, is not sufficiently rarefied to permit an electrical surge or brush discharge to take place between its two elements. However, the entrance of a quantum into this tube produces a temporary surge from cathode to anode. In the original instrument this surge was measured on the electrometer but since the advent of vacuum tube amplifiers, this small impulse is magnified electrically to sufficient strength to indicate on a loudspeaker or an impulse counter.

The tube is normally sensitive to roentgen radiation, gamma radiation, and cosmic radiation but if a thin window is placed in the tube to permit beta radiation and alpha particles to enter, it becomes sensitive to them.

When an impulse is started in the tube, it must be stopped by some mechanism in order to make the tube susceptible to the next impulse. Tubes can be built with certain gaseous characteristics making them self-quenching—others that do not have this characteristic are quenched by an external condenser and resistor.

The tube of the externally quenched type is a less expensive tube to build, and has an almost unlimited life, but it has the disadvantage of not being able to take impulses at a rapid rate. A tube of this type, therefore, will be perfectly satisfactory as a detecting instrument, as, for example, for the location of lost radium, and could be used for comparing relatively low intensities of gamma radiation where the radioactive sources could be placed at sufficient distances to bring the intensities well within the handling range of the tube. However, a tube of this kind would not be suitable for the measurement of beta radiation because normally the disintegrations come at too rapid a rate to permit a tube of this kind to handle them, and of course the sources of beta radiation could not be moved away greater distances because the high absorption taking place in air makes the law of inverse squares inapplicable. For the last mentioned purpose a self-quenching tube becomes necessary.

When alpha particles and beta radiation are to be measured by the tube, the window thickness is of great importance, and of course a tube with a thinner window intro-

duces greater manufacturing complications and hence increases the expense of construction. Most manufacturers rate their tubes by the weight in milligrams per square centimeter of window material.

When high intensities of radiation are being delivered to the tube the number of impulses becomes far too rapid to permit an observer to count them or to operate a mechanical counter, and for this reason, all of the more elaborate instruments have incorporated in them what is known as a scaling circuit, by which a radio tube receives one impulse and is rendered inoperable by the next impulse—a number of tubes being connected together in this manner are known by the unscientific, but at least descriptive, term of a "flip-flop" circuit. A circuit of this kind unfortunately does not give a decimal system of numeration, but records on a system of the powers of two; that is, 2, 4, 8, 16, 32, 64. As a rule, the mechanical register is made to operate only on every sixty-fourth count, the intermediate numbers being shown by a neon pilot light properly numbered on the dial.

Recently circuits known as the decade scaler have appeared on the market and if proved satisfactory, will greatly reduce the amount of figuring necessary in any particular operation.

Under most circumstances, the Geiger counter is used for the problem of comparing one intensity of radioactivity with another, in which case a known sample is placed at a convenient distance from the tube and impulses are counted over a reasonable length of time. Inasmuch as the base rate of count of the instrument from cosmic radiation or natural radioactivity is known, that number must be subtracted from the total number of counts received when the known sample is being tested. The unknown is then placed at a similar distance from the tube and the count made for the same length of time, the base rate again subtracted and the two numbers of counts are compared to each other as the values of radioactivity in the two samples. By this means a counter may be said to be calibrated.

Under certain circumstances a counter can be used as an absolute measure of radioactivity inasmuch as the counter gives one impulse for every disintegration which takes place in the radioactive material. However, it is difficult, if not actually impossible, to allow all of the disintegrations to influence the tube unless the radioactive material is actually placed within the tube. As it would obviously be impractical in most cases to place the radioactive sample within the tube, one must be content with allowing a known proportion of all the impulses to influence the tube. From a practical standpoint a small source of radioactive material, such as a drop of radiophosphorus in solution, evaporated on a piece of paper, can be placed directly on the window of the tube so that a hemisphere of radiation will enter the tube (half of all the disintegrations which are taking place). As a millicurie of radioactive material gives thirty-seven million disintegrations per second, the actual radioactivity of a sample can be determined by the impulse counter.

The Geiger tube may also be connected to what is known as a counting rate meter, in which case the individual impulses, instead of being recorded and counted, are fed into a condenser whose potential is determined by a meter. The meter can be calibrated so as to read directly in number of counts per minute. A meter of this type is not as accurate as an actual count of the impulses, but where readings must be taken rapidly and where the counter may be moved around to pick up the strongest point of radiation, as for example over the thyroid gland to determine the greatest concentration of radioiodine, it becomes an extremely handy instrument, which gives precise localizations.

Attention is called to the fact that a Geiger counter can give fair comparisons of radiation only when the qualities of the two types of radiation are the same. There-

fore, some caution should be used when a Geiger counter serves the purpose of a health survey meter because an instrument which is accurately calibrated in fractions of a roentgen for gamma radiation may give entirely false indications when used in the presence of beta radiation or roentgen radiation within the diagnostic range.

In general, counters may be classified as follows:

1. The simple battery-operated instrument indicating the presence of radium or roentgen radiation. This may indicate by means of earphones or a loudspeaker or a flashing lamp. It is used for the recovery of lost radium and it is very valuable for detecting radiation leaks and making protection surveys. In the battery-operated instrument the difficulty arises from the fact that a battery of 900 to 1,500 volts is an expensive, heavy and short-lived piece of equipment. A number of different types of electrical circuits have been developed to give this necessary voltage from a low voltage battery, but in general they are only reliable in the hands of a skilled operator. Where the instrument is to be used by persons totally unfamiliar with it, as would be necessary in civilian protection from atomic warfare, no substitute for the battery has been developed.

2. A scaling circuit meter whose scale may be either of the 64 or of the decade type. It is necessary for making high precision measurements in calculating dosage and studying body fluids or tissue sections.

3. A rate-of-count meter which does not have the accuracy but which is much more simple to use than a scaler circuit. It is used in making comparative measurements for establishing the function of living tissue and for making precise localizations of aberrant or metastatic lesions in the living patient.

In any of the above-mentioned counters, the window thickness of the tube must depend on the type of radiation to be encountered.

Consideration of the above factors should show the radiologist that when he asks what type of counter is the best to purchase, he must qualify this question by a statement as to its intended use.

It is also well to keep in mind that the performance of any complicated piece of equipment is seldom better than the skill of the operator.

Robert B. Taft, M.D.

THE REGISTRY OF RADIOLOGICAL PATHOLOGY

THE Registry of Radiological Pathology is an excellent example of cooperation between the major organizations of the radiologists of North America, and shows what may be accomplished when a worthy cause is presented to them. The American Registry of Pathology has for many years served as a central file for interesting and instructive pathological material from many specialties and has proved its worth to the participating societies. There has been an increasing feeling that radiology should have its place in the Registry. The American College of Radiology, the American Roentgen Ray Society and the Radiological Society of North America have agreed to support a Registry of Radiological Pathology for a trial period. Additional details regarding fellowships at the Registry appear in an announcement in this issue of the Journal in the Department of Correspondence.

THOMAS RAYMOND HEALY
1879–1948

DR. THOMAS RAYMOND HEALY died in the Anna Jaques Hospital in Newburyport, Massachusetts, on February 25, 1948. He had served on the senior staff continuously from 1900 to 1946, when he was retired for age. No other doctor had served the hospital so long.

Dr. Healy was born in Newburyport. He played on the first football team of the Newburyport High School. After graduation from Dartmouth Medical School in 1899, he went into practice with his father, Dr. James J. Healy. His first instructor in roentgenology was the immortal Walter

Dodd. In 1908 he founded the radiological department of the Anna Jaques Hospital, with his own machine. In 1917 he was called to active duty with the Navy, and was made chief radiologist to the Marine Corps; he served at Belleau Wood and Chateau Thierry. The following year he was transferred back to the Navy, and made chief of all X-ray departments of the Navy in France. Later in that year he was assigned to the Chelsea Naval Hospital. In 1920 he was transferred to the Fleet Reserve as medical officer for the first battalion, at the Boston Navy Yard, At the beginning of World War II, Dr. Healy was made commanding officer of the Naval Base Hospital. He was roentgenologist at the Naval Training Station at Newport, Rhode Island, for over a year, and attained the rank of captain.

Dr. Healy was a member of many medical societies. He practiced in Newburyport and in Boston. He served as president of the New England Roentgen Ray Society and the Essex North Medical Society. He was a past commander of Newburyport Post of the American Legion and of the Massachusetts Naval Order and a past vice-commander of the National Naval Order. He was well known as a sportsman. His yacht Ida J. was the champion of her class in New England. He was a member of the Corinthian Yacht Club of Marblehead and of the American Yacht Club. He also owned a racing speedboat. In the bicycle age, he was an active participant, frequently riding a hundred miles. He drove his thirty year old Stutz in 1947 in a revival of the Glidden Tour.

He was a member of the Holy Name Society of the Immaculate Conception Parish, where a solemn requiem high mass was held. He was also a member of the Knights of Columbus, of the Elks, and of the Ancient and Honourable Artillery Society.

Dr. Healy never married. He is survived by a brother, James J. Healy, of Weymouth; by a nephew, Major James K. Healy, of Newburyport, and by a niece, Mrs. Whitefield Kimball of Manchester, Massachusetts.

Ramsay Spillman

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Palmer House, Chicago, Ill., Sept. 14–17, 1948.

American Radium Society
Secretary, Dr. H. F. Hare, 605 Commonwealth Ave., Boston, Mass. Annual meeting: 1949, to be announced.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Hotels Fairmont and Mark Hopkins. San Francisco, Calif., Dec. 5–10, 1948.

American College of Radiology
Secretary, Mac F. Cahal, 20 N. Wacker Drive, Chicago 6. Annual meeting: 1949, to be announced.

Section on Radiology, American Medical Association
Secretary, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio, Annual Meeting: 1949, to be announced.

Alabama Radiological Society
Secretary, Dr. C. S. Stickley, 515 Bell Bldg., Montgomery, Ala. Next meeting time and place of Alabama State Medical Association.

Arkansas Radiological Society
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Brooklyn Roentgen Ray Society
Secretary, Dr. A. H. Levy, 1354 Carroll St., Brooklyn 13, N. Y. Meets monthly on fourth Tuesday, October to April.

Buffalo Radiological Society
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse, N. Y. Three meetings a year January, May, November.

Central Ohio Radiological Society
Secretary, Dr. Paul D. Meyer, Grant Hospital, Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Seneca Hotel, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. T. J. Wachowski, 310 Ellis Ave., Wheaton, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. Eugene L. Saenger, 735 Doctors Bldg., Cincinnati 2, Ohio. Meets last Monday of each month, September to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. George L. Sackett, 10515 Carnegie Ave. Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

Denver Radiological Club
Secretary, Dr. Mark S. Donovan, 306 Majestic Bldg., Denver 2, Colo. Meets third Friday of each month at Department of Radiology, Colorado School of Medicine.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

Florida Radiological Society
Secretary, Dr. J. A. Beals, St. Luke's Hospital, Jacksonville, Fla. Meets twice yearly, in April preceding annual meeting of Florida Medical Society, and in November.

Georgia Radiological Society
Secretary, Dr. Robert Drane, DeRenne Apartments, Savannah, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

Houston X-ray Club
Secretary, Dr. Curtis H. Burge, 3020 San Jacinto St., Houston 4, Texas. Meets fourth Monday each month.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. J. A. Campbell, Indiana University Hospitals, Indianapolis 7. Meets second Sunday in May.

Iowa X-Ray Club
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

Kansas Radiological Society
Secretary, Dr. Anthony F. Rossitto, Wichita Hospital, Wichita, Kansas. Meets annually with the State Medical Society.

Kentucky Radiological Society
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

Long Island Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. Moris Horwitz, 441 No. Camden Drive, Beverly Hills, Calif. Meets second Wednesday each month at Los Angeles County Medical Assn. Building.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

Louisville Radiological Society
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Louisville General Hospital.

Michigan Association of Roentgenologists
Secretary, Dr. R. D. McDuff, 220 Genesee Bank Bldg., Flint 3, Mich.

Milwaukee Roentgen Ray Society
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave.,

* Secretaries of societies not here listed are requested to send the necessary information to the Editor.

Milwaukee, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
Secretary, Dr. Chauncey N. Borman, 802 Medical Arts Bldg., Minneapolis 2, Minn. Two meetings yearly, one at time of Minnesota State Medical Association the other in the fall.

Nebraska Radiological Society
Secretary, Dr. Ralph C. Moore, Nebraska Methodist Hospital, Omaha 3, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

New Hampshire Roentgen Ray Society
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

New York Roentgen Society
Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

North Carolina Radiological Society
Secretary, Dr. J. E. Hemphill, 323 Professional Bldg., Charlotte 2, N. C. Meets in May and October.

North Dakota Radiological Society
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings held by announcement.

Northern California Radiological Club
Secretary, Dr. C. E. Grayson, Medico-Dental Bldg., Sacramento 14, Calif. Meets at dinner last Monday, every second month, except June, July and August. Next meeting Sept. 27, 1948.

Ohio State Radiological Society
Secretary, Dr. Carroll C. Dundon, 2065 Adelbert Road, Cleveland 6, Ohio.

Oklahoma State Radiological Society
Secretary, Dr. W. E. Brown, Tulsa, Okla. Three regular meetings annually.

Oregon Radiological Society
Secretary, Dr. William Y. Burton, 242 Medical Arts Bldg., Portland 5, Oregon. Meets monthly 2nd Wednesday, 8:00 P.M., Library of University of Oregon Medical School.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

Pacific Northwest Radiological Society
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport.

Philadelphia Roentgen Ray Society
Secretary, Dr. Arthur Finkelstein, Graduate Hospital, 19th and Lombard St. Meets first Thursday each month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. R. P. Meader, 4002 Jenkins Arcade Pittsburgh 22, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

Queens Roentgen Ray Society
Secretary, Dr. J. E. Goldstein, 88-29 163rd St., Jamaica 3, N. Y. Meets fourth Monday of each month except during the summer.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Harry A. Miller, 2452 Eutaw Place, Baltimore. Meets third Tuesday each month, September to May.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Robert M. Lowman, Grace-New Haven Community Hospital, New Haven 11. Meets bimonthly second Thursday, at place selected by Secretary.

Radiological Section, District of Columbia Medical Society
Secretary, Dr. A. A. J. Den, 1801 K St., N. W., Washington, D. C. Meets Medical Society Auditorium, third Thursday, January, March, May, October at 8:00 P.M.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Radiological Society of New Jersey
Secretary, Dr. Raphael Pomeranz, 31 Lincoln Park, Newark, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Murray P. George, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr. Meets Salt Lake City, Utah, at Hotel Utah, Aug. 12, 13, 14, 1948.

St. Louis Society of Radiologists
Secretary, Dr. Edwin C. Ernst, Beaumont Medical Building, St. Louis, Mo. Meets fourth Wednesday of each month, except June, July, August, and September.

San Diego Roentgen Society
Secretary, Dr. R. F. Niehaus, 1831 Fourth Ave., San Diego, Calif. Meets monthly, first Wednesday at dinner.

Section on Radiology, California Medical Association
Secretary, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. Edwin L. Rypins, 427 N. Main St., Bloomington, Ill.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

Utah Radiological Conference
Secretary, Dr. Henry H. Lerner, School of Medicine, University of Utah, Salt Lake City 1. Meets 1st and 3rd Thursdays monthly from 7:30 to 10 P.M., Salt Lake County General Hospital, September to June.

Utah State Radiological Society
Secretary, Dr. M. Lowry Allen, Judge Bldg., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Homer V. Hartzell, 310 Stimson Bldg., Seattle 1, Wash. Meets fourth Monday each month, October through May, College Club, Seattle.

X-Ray Study Club of San Francisco
Secretary, Dr. Ivan J. Miller, 2000 Van Ness Ave. Meets monthly on third Thursday at 7:45 P.M., first six months of year at Lane Hall, Stanford University Hospital, and second six months at Toland Hall, University of California Hospital.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Mexico

Sociedad Mexicana de Radiologia y Fisioterapia
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

British Empire

British Institute of Radiology Incorporated with the Roentgen Society
Medical Members' meeting held monthly on third Friday at 2:30 P.M. and Ordinary Meeting at same time on following Saturday, October to May, 32 Welbeck St., London, W.1.

Faculty of Radiologists
Secretary, Dr. M. H. Jupe, 23 Welbeck St., London, W.1 England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary, Dr. E. M. Crawford, 2100 Marlowe Ave., Montreal 28, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Francaise d'Electrologie et de Radiologie Médicales
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

Australian and New Zealand Association of Radiologists
Honorary Secretary, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
Honorary Secretaries, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. L. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. B. C. Smeaton, 178 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179-B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

South America

Sociedad Argentina de Radiologia
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Andrelino Amaral, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Tuesday at 9 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado, 2306 Lima, Peru. Meetings held monthly except during January, February and March, at the Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Continental Europe

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 111 Avenue des Alliés, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Ceskoslovenská společnost pro röntgenologii a radiologii v Praze
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Next meeting May 13 and 14, 1948.

Gdansk Section, Polish Society of Radiology
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10.30, X-Ray Dept., Akademia Gdansk.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad.
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
President, Dr. H. E. Walther, Gloriastr. 14, Zürich, Switzerland.

FELLOWSHIPS OF THE REGISTRY OF RADIOLOGICAL PATHOLOGY

The Registry of Radiological Pathology has been established through the cooperation and support of the American College of Radiology, the American Roentgen Ray Society and the Radiological Society of North America. This Registry is part of the American Registry of Pathology which, in turn, is one of the four divisions of the Army Institute of Pathology and the only division which operates under the auspices of the National Research Council. The Registry is housed in the same building as the Army Medical Library (formerly known as the Surgeon General's Library).

Fellowships in several other specialties are supported at the Institute of Pathology by organizations sponsoring registries; e.g., the American Academy of Ophthalmology, the American Academy of Orthopedic Surgeons, etc. There are over fifteen specialty registries included in the American Registry of Pathology. In the case of the Registry of Radiological Pathology, the American College of Radiology supplies funds to the National Research Council for general expenses. The American Roentgen Ray Society and the Radiological Society of North America each supports two six-month Fellowships annually which carry monthly stipends of $250.00 per Fellow. The four Fellows thus supported receive appointments starting January 1, April 1, July 1 and October 1, respectively, in order that two Fellows may work together and that continuity of effort may be maintained by a three-months' overlapping of appointments. The work of the Fellows is supervised and coordinated by civilian consultants chosen by the Director of the Institute of Pathology. The consultants are currently Dr. L. H. Garland, San Francisco, California, Dr. Fred J. Hodges, Ann Arbor, Michigan, and Dr. Merrill C. Sosman, Boston, Massachusetts.

Applications are now open for the Fellowships. The American Roentgen Ray Society Fellowships begin July 1 and January 1, and the Radiological Society Fellowships on October 1 and April 1.

In order to facilitate the establishment of the Registry, the American Roentgen Ray Society and the Radiological Society of North America have appointed Fellows who are now working at the Registry. The following outline of their activities to date indicates the nature of the Fellowships:

OUTLINE OF FACILITIES AND ACTIVITIES OF FELLOWS AT THE REGISTRY OF RADIOLOGIC PATHOLOGY

I. Schedule for routine daily activities.
   - A. Study of the histopathological slide sets prepared by the American Registry of Pathology. One and one-half to two hours is suggested.
     1. There are thirty-six such sets, two of which cover general pathology and the remainder cover specific subjects.
     2. Supervision by a staff pathologist is made available for the Fellow.
   - B. Study of roentgenographic teaching aids already prepared.
   - C. Attendance at the three weekly conferences of the professional staff of the Institute. At these conferences both typical and unusual cases are presented. The clinical history, physical and roentgenological findings are presented, the gross specimen demonstrated and the histopathological findings demonstrated by projection.
   - D. Attendance at radiological conferences at various Washington hospitals. These include Walter Reed Hospital, Garfield Memorial Hospital and Doctors Hospital.
   - E. Consultation with members of the Institute Staff on cases having roentgenograms.

II. The preparation of roentgenographic material at the Registry for teaching aids.
   - A. This activity includes two phases:
     1. The addition to such atlases as have been prepared by previous Fellows. This would be done

from current cases as they are added to the Registry as well as from material reviewed by the Fellow through his other activities.

2. The preparation of material on a subject of the Fellow's own choosing (the choice to be approved by the Registry Committee). It should be emphasized that this provides an excellent opportunity for the Fellow to investigate a problem in which he may have a personal interest and at the same time fulfill his obligation to the Registry. Facilities for this type of work are excellent.

III. The Fellow is called upon to assist other members of the staff in consultation on radiologic aspects of their problems and investigations. By the same token, the Fellow may avail himself of advice on the pathologic aspects of his studies.

The majority of the cases now on file at the Institute of Pathology do not include roentgenograms of satisfactory quality for adequate correlation of roentgenologic and pathologic findings. This is largely due to the fact that continuous radiological consultation has not previously been available for the assembly of material. One of the chief obligations of the radiological Fellows is to correct this fault as far as possible by cooperating with the Institute Staff. The completeness of the Registry will depend to a large extent on the cooperation of the radiologists of the United States in sending worthwhile, completely documented cases to be included in the file.

The Registry Committees which will act as advisers of the Registry and select candidates for Fellowship are as follows:

American Roentgen Ray Society

Dr. Vincent W. Archer, Chairman
Dr. Lyell C. Kinney
Dr. Leo G. Rigler
Dr. Merrill C. Sosman
Dr. Paul C. Swenson

Radiological Society of North America

Dr. Frederick W. O'Brien, Chairman
Dr. John D. Camp
Dr. Robert S. Stone

Applications for Fellowship may be obtained by writing to the Chairman of either of the above committees. Application should be made to only one committee and will receive due consideration by either or both of the committees. Final approval of all Fellows rests with the Director of the Institute of Pathology.

Details regarding the Registry of Radiological Pathology, its aims and the steps which led to its establishment may be obtained by writing to Mr. Mac F. Cahal, Secretary, American College of Radiology, 20 North Wacker Drive, Chicago, Illinois.

AMERICAN BOARD OF RADIOLOGY

The fall examination of the American Board of Radiology will be held at the Hotel Floridan, Tampa, Florida, November 1–5, inclusive, 1948. The Southern Medical Association is holding its annual meeting in Miami, Florida, October 25–28, 1948, and the annual Cancer Seminar of the Southeastern States will be held in Tampa on November 8, 9 and 10, 1948. This Seminar is sponsored by the American Cancer Society, Florida Division, and the Florida State Board of Health. A large attendance of physicians is expected. It is hoped that as many candidates as possible can attend both the Southern Medical Association meeting in Miami and the Cancer Seminar in Tampa. All those hoping to be examined in Tampa should have their applications on file with the Secretary not later than September 1, 1948.

B. R. Kirklin, M.D., Secretary
Mayo Clinic
Rochester, Minnesota

RESEARCH FELLOWSHIPS—AMERICAN COLLEGE OF PHYSICIANS

The American College of Physicians announces that a limited number of Fellowships in Medicine will be available from July 1, 1949–June 30, 1950. These Fellowships are designed to provide an oppor-

tunity for research training either in the basic medical sciences or in the application of these sciences to clinical investigation. They are for the benefit of physicians who are in the early stages of their preparation for a teaching and investigative career in Internal Medicine. Assurance must be provided that the applicant will be acceptable in the laboratory or clinic of his choice and that he will be provided with the facilities necessary for the proper pursuit of his work.

The stipend will be from $2,200 to $3,200.

Application forms will be supplied on request to the American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa., and must be submitted in duplicate not later than November 1, 1948. Announcement of the awards will be made as promptly as is possible.

THE AMERICAN COLLEGE OF PHYSICIANS ANNOUNCES ITS ANNUAL 1949 SESSION

The American College of Physicians will conduct its Thirtieth Annual Session at New York, New York, March 28 through April 1, 1949. Dr. Franklin M. Hanger, Jr., of New York City is the Chairman for local arrangements and the program of Clinics and Panel Discussions. The President of the College, Dr. Walter W. Palmer, Director of the Public Health Research Institute of the City of New York, Inc., and Professor Emeritus, Columbia University College of Physicians and Surgeons, is in charge of the program of Morning Lectures and afternoon General Sessions.

Secretaries of medical societies are especially asked to note these dates and, in arranging meeting dates of their societies, to avoid conflicts with the meeting of the American College of Physicians, for obvious mutual benefits.

TWENTY-FIRST ANNIVERSARY YEAR OF *HAROFE HAIVRI*

The Hebrew Medical Journal

The appearance of Volume I, 1948, of the *Harofe Haivri, The Hebrew Medical Journal,* inaugurates the twenty-first successful year of its publication under the editorship of Moses Einhorn, M.D. The Journal's contents is not confined to technical medical topics but is divided into several sections covering a variety of related subjects of interest to the medical profession.

The founders had faith in the vitality and growth of modern Hebrew and foresaw that a Hebrew medical publication would be of service to the future medical department of the Hebrew University and of great value in the development and advancement of Hebrew medical literature.

The section on Palestine and Health contains an article by A. Klopstock, M.D. which discusses the high incidence of Amoebiasis in Palestine. Included also is the significant study of Mental Health in Palestine by A. H. Merzbach, M.D., and a survey of the Present Urological Conditions in Palestine by W. Boss, M.D. Dr. M. Buchman describes the history of the Hot Springs of Tiberias and presents a full analysis of their therapeutic value.

In the section on Historical Medicine, Dr. M. Gelber reviews the contribution of the Jewish doctors in Poland during the eighteenth century. The section on Personalia contains a biographical sketch of Dr. I. Seth Hirsch, and his contributions to the field of radiology.

The original articles are summarized in English to make them available to those who are unable to read Hebrew.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

SKELETAL SYSTEM

Barnhard, Leonard, and Stubbins, Sam G. Styloidectomy of the radius in the surgical treatment of non-union of the carpal navicular; preliminary report. *J. Bone & Joint Surg.*, Jan., 1948, *30-A*, 98–102.

The surgical removal of the radial styloid is presented in this paper as an aid in the treatment of malunited and ununited fractures of the carpal navicular. The authors believe the removal of the styloid process simplifies the surgical approach and ensures better visualization and immobilization of the fragments of the fracture, as well as less likelihood of secondary degenerative changes. By employing the excised styloid fragment for grafting material, the whole operative procedure can be confined to a single operative field.—*R. S. Bromer.*

Rodholm, A. K., and Phemister, Dallas B. Cyst-like lesions of carpal bones, associated with ununited fractures, aseptic necrosis, and traumatic arthritis. *J. Bone & Joint Surg.*, Jan., 1948, *30-A*, 151–158.

The authors state it is a matter of common knowledge that cyst-like areas of bone absorption occur about the hip in degenerative conditions of the joint. Few references to the occurrence of such lesions about the wrist in degenerative conditions of the radiocarpal and carpal joints, are to be found in medical literature, although such lesions are not uncommon.

Three cases are reported. In the first, the roentgenograms of the wrist showed a large cyst-like area of central absorption in the capitate, and a smaller area in the triangular bone. There was no sclerosis of the surrounding shell of bone. The cartilage of the radionavicular articulation was narrowed, and the cortex of the bone was obscured. In the second, on roentgenographic examination, a cyst-like area, without sclerosis about it was shown in the proximal two-thirds of the capitate. The navicular was in two parts, due to old fracture, the proximal portion being narrowed and deformed. There apparently had been aseptic necrosis of the proximal fragment with subsequent collapse and secondary arthritis. In the third patient, an old fracture of the navicular was demonstrated with, however, no evidence of necrosis of the proximal fragment. There was cystic rarefaction of the lunate, with a shell of sclerotic bone about the cyst. A small loose body was noted near the navicular, and there were tiny osteophytes along the articular surface of the radius.

The changes undergone by necrotic bone and cartilage, following interruption of the blood supply to the head of the femur, have been described. The necrotic epiphysis may undergo progressive and complete replacement by living bone. Usually, replacement is incomplete and irregular. Areas of necrotic bone may be absorbed and replaced by fibrous tissue, without subsequent replacement by living bone. These are the cysts seen late in the process. Articular cartilage degenerates and is replaced to a varying degree by fibrocartilage and fibrous tissue.

Pathologically, the cyst-like areas of rarefaction in the carpal bones resemble the cysts of the capital femoral epiphysis, and their pathogenesis may be assumed to be essentially the same. They also bear some resemblance to subcortical cyst-like areas in the femoral head and in the acetabulum at the weight-bearing region in chronic degenerative arthritis. The severity of symptoms in these cases is probably dependent upon the severity of the associated degenerative arthritis. Surgical treatment is beneficial, but, the authors believe, cannot be expected to provide complete relief from symptoms.—*R. S. Bromer.*

Fairbank, H. A. Thomas. Osteogenesis imperfecta and osteogenesis imperfecta cystica. *J. Bone & Joint Surg.*, Feb., 1948, *30-B*, 164–186.

In this paper, a short concise description of osteogenesis imperfecta is given which includes the clinical and histopathological findings and roentgenographic appearance together with case reports and roentgenograms of 12 cases.

Three groups of cases are defined by their roentgenographic appearance:

Type 1. Thick bone type. These are severe prenatal cases, born with limbs which are stunted as in achondroplasia and with numer-

ous fractures, notably in the ribs. The major long bones are short and are usually broad and thick, and show one or more fractures with ample callus. The proximal segments of the limbs, the femora and humeri, are most severely affected, but the tibias may also be enlarged. It may be seen up to three months after birth but is seldom met with later.

Type 2. Sender, fragile bone type. This condition is seen in prenatal cases which survive more than a few months, and in all postnatal cases. The skeleton as a whole is osteoporotic and the long bones are usually slender. The cortex is characteristically thin and of deficient density. The extremities of the bone often appear large, and in older children they may show varying degrees of honeycombing. Occasionally the shafts of some long bones, perhaps after repeated fracture, may be slender and yet surprisingly dense as compared with the ends of the bones. Deformities due to fracture or bending are common. Transverse lines of dense bone, straight or wavy, often mark the ends of the metaphyses. The skull is thin and wormian bones may be present. The vertebral bodies are translucent, shallow spread, and biconcave and the intervertebral discs are biconvex.

Type 3. Osteogenesis imperfecta cystica. This name is suggested for cases with pronounced honeycombing of the bones and is extremely rare. The condition dates from birth, and is definitely progressive. Cystic changes which are more pronounced in the lower than in the upper limbs become increasingly evident with advancing years. Deformity due to fracture and bending of bone is progressive. In the 2 cases reported in the paper the scleras were not blue. The condition differs from multiple diffuse fibrosis of bone in that bone changes occur much earlier, the roentgenographic appearances are not really similar and the histopathological appearances are quite different.—*R. S. Bromer.*

Sherman, Mary S. Osteoid osteoma; review of the literature and report of thirty cases. *J. Bone & Joint Surg.*, October, 1947, *29*, 918–930.

The literature of osteoid osteoma is first reviewed. Included in the series of 30 cases is 1 previously reported by Phemister as a case of "chronic fibrous osteomyelitis" and 2 reported by Compere previously, as *Streptococcus viridans* osteomyelitis. The clinical picture is given in detail with emphasis on the age incidence, and on location of the lesions. In the author's series, over half the patients were between the ages of five and fifteen years. The location of the lesions corresponded well with those given in the literature, with, however, one noteworthy exception, namely, almost 25 per cent were situated in the spine. The chief physical finding was tenderness which usually was definitely localized and which was at times exquisite. Involvement of a lower extremity usually produced a limp and atrophy of the muscles. In the spine, the lesion produced all the signs of acute localized back pain, including muscle spasm, secondary scoliosis and pelvic tilt. If the lesion was present long enough, there was usually palpable thickening of the bone. Lesions in bones with little soft tissue covering were accompanied by swelling, but this area was rarely warm and never red. There were no systemic complaints.

Roentgenographic examination of a mature lesion revealed a characteristic picture. The active nidus was usually a small round or oval area of reduced density. Often one could see within it a small dense shadow which represented ossification of the central portion. About this nidus, a thick, dense shadow of sclerotic regional bone was almost always present. If the lesion was at or in the cortex, the regional hypertrophy, especially along the periosteal surface, was much greater. If the circumference of the shaft was much increased and the bone was sclerotic, the nidus was difficult to demonstrate in the roentgenogram.

The weight of evidence is regarded by the author as against infection as the cause of the lesion. Osteoid osteomata, unlike other benign tumors, are never larger than 1 cm. or so in diameter. Once they have reached a mature state they do not grow, although the hypertrophied regional bone may increase to form a large mass. Furthermore, it is not unusual for benign tumors to be painful, but the pain of osteoid osteomata is out of proportion to their small size. After consideration of all the facts, the author is in agreement with Jaffe that the lesion is not of infectious origin, but is probably best interpreted as a benign tumor.—*R. S. Bromer.*

Lumb, George, and Prosser, T. M. Plasma cell tumors. *J. Bone & Joint Surg.*, Feb., 1948, *30-B*, 124–152.

This review is based on the study of 15 cases. The authors attempt to demonstrate the various manifestations of plasma cell tumors. The

term multiple myelomatosis is used in the paper when a number of bones are involved. Single tumors are described as solitary plasmocytomas, either of the bone marrow or of soft tissue according to their origin. They also correlate their cases with the others already reported in the literature and thus make a comprehensive classification of the disease.

The disease process is divided as follows into three groups:

1. Bone Marrow Tumors
   (a) Multiple at onset.
   (b) Solitary at onset, with subsequent multiple spread.
   (c) Solitary bone marrow tumors.
2. Extramedullary Tumors
   (a) Confined to the nasopharynx.
   (b) Primary in nasopharynx but associated with lymph node involvement.
   (c) Primary in nasopharynx but associated with bone marrow involvement.
   (d) Very rare examples occurring in other tissues, i.e., pleura, testes, skin, etc.
   (e) Confined to the conjunctiva (a somewhat doubtful group probably of granulomatous origin).
3. Generalized Spread (from 1 or 2 above)
   (a) Spread to viscera, liver, spleen, etc.
   (b) Plasma cell leukemia.

In the paper the literature is reviewed, case examples are quoted to show the gradual merging of the different clinical and pathological syndromes into one entity, and a comprehensive analysis of the various manifestations of the disease is made.

The roentgenographic appearance in typical cases of multiple myelomatosis is characterized by multiple circumscribed areas of destruction involving both the cortex and the medulla in which the bone texture has completely disappeared. The lesions occur in any part of the bone and typically they are found in vertebrae, ribs, sternum and skull, eventually affecting any or all bones of the skeleton. The areas appear as clear-cut, punched-out oval or round patches of complete translucency from 1 to 3 cm. in diameter, a characteristic feature being the lack of new bone formation either in the bone itself or in the periosteum. Fractures and, when the lesion is in the vertebrae, areas of collapse are common. Collapse of vertebrae occurs at an early stage and is associated with destruction of the intervertebral disc, in contradistinction to metastatic carcinoma where collapse occurs later and the discs are not involved. Kyphotic deformities are frequent, and differentiation from tuberculosis of the spine may be difficult insofar as this disease is also characterized by destruction of the intervertebral disc. Deficiencies in the skull often simulate those seen in xanthomatosis, but this condition is most frequent in children and young people, and the deficiencies have an irregular outline forming "map-like" appearances. Translucent areas in the skull are also found in osteomalacia and osteitis fibrosa which must be excluded.

Two different types of solitary plasmycytomas of bone marrow are shown in the roentgenogram. Both have essentially identical histological changes. The first type is cystic and resembles an osteoclastoma. The lesion is usually large, of reduced density, and sharply limited; within it are thickened irregular trabeculae. It is usually found in the medullary portion of the pelvis or long bones, frequently expanding the cortex, and pathological fractures may occur.

The second type of lesion is purely destructive and has an appearance very similar to the osteolytic metastasis of a carcinoma, or an osteolytic type of osteogenic sarcoma. It is sharply demarcated, homogeneously rarefied in appearance, and seldom shows expansion. The vertebrae are often involved. The first type is the rarer form.

The finding of plasma cells in the peripheral blood stream is unusual but has been recorded in cases of multiple myelomatosis. Where plasma cells are a constant feature in the peripheral blood stream, in association with other signs of myelomatosis such as Bence-Jones proteinuria and bone marrow invasions, the term plasma cell leukemia is used. The generalized nature of the disease and its course are similar to that seen in other leukemias.

The authors consider that metastasis plays no part in the disease process. They believe the variety of forms of plasma cell tumors which they demonstrate and correlate with the others described in the literature are gradations of an essentially similar process and should not be regarded as separate conditions. The disease should be regarded as of multifocal origin as opposed to any theory of spread by metastasis. No dogmatic statement can be made as to the exact origin of the cells in the plasma cell tumors.—*R. S. Bromer.*

Ciccone, Roy, and Richman, Robert M. The mechanism of injury and the distribution of three thousand fractures and dislocations

caused by parachute jumping. *J. Bone & Joint Surg.*, Jan., 1948, *30-A*, 77–97.

This paper describes a series of 3,000 fractures and major soft part tissue injuries resulting from parachute jumping, with particular reference to the traumatic mechanisms involved. The injuries showed a strong predilection for weight-bearing structures; the foot and the ankle, the leg, femur and spine together accounting for 90 per cent of the series. The relative frequency of certain injuries, however, is different from that encountered in civilian orthopedic practice. The series included few fractures of the calcaneus and of the distal end of the radius although both are associated with the trauma of falling. Fractures of the posterior margin of the tibia and multiple metatarsal fractures on the other hand were disproportionately prevalent among parachutists. No injury was specific enough to be called a typical parachute lesion.

Almost all the injuries of parachute jumping can be attributed to four basic mechanisms according to the authors:

(a) Torsion plus landing thrust. This is by far the most common mechanism of injury and is responsible for a chain of related injuries extending from the toes to the hip.

(b) Backward landing. Vertebral compression fractures and head injuries characterize this mechanism of injury.

(c) "Opening shock." This is a mechanism peculiar to parachute jumping. The violent abduction stress causes many ligamentous tears and even fractures of the extremities.

(d) Violent vertical landings. Occasional parachute malfunctions increase the landing impact and cause severe multiple fractures of the legs and spine.

One-half of all parachute fractures of the series involved the ankle mortise. The most prevalent mechanism was external rotation which, together with abduction, accounted for approximately 75 per cent of the fractures at the ankle. The entire lower extremity showed a preponderance of external rotation injuries which would imply a structural weakness of the limb as a whole,—a lack of adaptive resiliency to the stress of external torsion.

The authors regard a classification of fractures based on etiological stresses as much more reasonable than one based on anatomical location. Recognition of the etiological stresses not only relates apparently dissimilar fracture patterns, but also provides a rational approach to treatment.—*R. S. Bromer.*

Fletcher, Gilbert H. Backward displacement of the fifth lumbar vertebra in degenerative disc disease. *J. Bone & Joint Surg.*, Oct., 1947, *29*, 1019–1026.

This paper is based on a study of 600 roentgenograms of the spine, taken on male subjects in the Medical Department of the Veterans Administration Pittsburgh Regional Office. Almost 90 per cent of the patients in the series were less than forty years of age. The universal symptom was backache, most often in the low back; limitation of motion and sciatica were commonly associated complaints. All of the roentgenograms were exposed with the patient in the recumbent position.

Fletcher confirmed the observation of Willis from measurements of skeletons, namely, that there is often a difference in the diameters of the fifth lumbar and first sacral vertebrae. This difference existed in 87 per cent of the cases with backward displacement, and in practically none of the control group. This difference in diameters was found to account for only about one-half of the apparent backward displacement in 85 per cent of the cases of the series, thus disproving the suggestion of Willis that such displacement is only an optical illusion.

Backward displacement is usually associated with degenerative changes in the posterior fibers of the annulus fibrosus and a high incidence of advanced degenerative disc disease Fletcher thus believes that there is a correlation between differences in diameters and disc disease. He found that there is no exaggeration of the lumbosacral angle in backward displacement. The lower lumbar and the upper sacral facets are of frontal or predominantly frontal type, and are in a plane directed downward and backward. The cause of backward displacement lies in the narrowing of the disc. The slipping of the inferior facets of the fifth lumbar vertebra, due to narrowing of the disc, cannot but take place in a downward and backward direction, carrying the entire body of the fifth lumbar backward in its relationship to the first sacral segment. Degenerative disc disease or degenerative changes in the posterior aspect of the annulus fibrosus come first, and posterior displacement is a mechanical consequence. The displacement is greater when the roentgenograms are exposed with the spine in hyperextension; this is due to the fact that hyperextension exaggerates the overriding of the facets and brings out the joint instability.

The differentiation of disc herniation from degenerative disc disease is of great therapeutic

importance because, in disc disease, there is no herniated material to remove for the purpose of alleviating pressure on nerve roots. This explains in great part poor results after surgery. Instead, it would seem logical, in the presence of disc disease and actual backward displacement, to fuse the lumbosacral joint with the lumbosacral junction in hyperflexion, in order to reduce the vertebral slipping as much as possible, and to improve the width of the intervertebral foramina.

When the roentgenologist finds a malalignment of the fifth lumbar with the first sacral vertebra, the lower border of the fifth lumbar and the upper border of the first sacral, as well as the amount of malalignment, should be measured. If the malalignment exceeds the difference in diameters, there is actual backward displacement. Careful scrutiny of the apophyseal joints shows overriding of the facets and eventually impingement upon the pedicles or laminae. A narrowing of the posterior aspect of the lumbosacral disc is commonly found and its significance is controversial; but, when associated with signs of instability, it can be inferred that degenerative changes are taking place.—*R. S. Bromer.*

LACHAPÈLE, A. P. Étude critique des rhumatismes chroniques vertébraux. (A critical study of chronic vertebral rheumatism.) *J. de radiol. et d'électrol.*, 1946, *27*, 285–312.

This excellent paper, actually a twenty-seven-page monograph splendidly illustrated, was presented at the IV Congress of French-speaking Radiologists held in Paris, October, 1946. The essay is divided into four sections:

I. Classical Conception of Chronic Vertebral Rheumatism with consideration of the following types:

1. Spondylitis rhizomelique (Marie-Strümpell)
2. Chronic rheumatic spondylosis with osteophytes (J. Teissier)
3. Traumatic spondylitis (Kümmell-Verneuil)
4. Spondyloarthritis (all types of infectious spondylitis)
5. Chronic rheumatic changes of the spine at present poorly classified
   a. Hereditary—traumatic kyphosis of Bechterew
   b. Fibrous spondylosis—resembling sp. rhisomelique but with long periods of complete arrest of disease during its course (a single proved case—Raymond and Babonneix)
   c. Arthritic changes about apophyseal joints
   d. "Vertical gout"—due to endocrine affects from thyroid and ovary (?)

II. Analysis of the above types of vertebral disease from study of clinical and roentgenological material. Here a meticulous description is presented of the many types listed above together with reproductions of roentgenograms (both clinical and of anatomical material).

III. Rheumatic pains viewed from the standpoint of anatomy and physiology of the spine—Their pathogenesis. Here lumbago and sciatic types of pain are considered from all anatomical physiological (metabolic, endocrine, biochemical), and embryological points of view.

IV. Conclusions—The practical clinico-roentgenological features of ankylosing spondylitis; traumatic infectious and degenerative forms of vertebral disease with osteophyte production; and the physiological approach to the explanation of backache are re-emphasized. The author ends by calling attention to a quotation by A. Léri placed at the head of the essay and which is applicable in explaining the large gaps in our knowledge of this field of pathology—"In pathology, certain terms have a charm which they do not merit. A qualificative poorly chosen is often adopted by the mass of physicians with an eagerness which the originator himself could not have surmised. The error then lies heavily at the feet of a belief based on preconceived convictions of some investigators, thereby limiting their powers of observation."

To the reviewer of this article the quotation seemed particularly appropriate to the subject of arthritis in general and chronic rheumatic lesions of the spine in particular.—*William M. Loehr.*

MARTIN, PAUL H. Slipped epiphysis in the adolescent hip; a reconsideration of open reduction. *J. Bone & Joint Surg.*, Jan., 1948, *30-A*, 9–18.

Martin describes the operation used by him for slipping of the femoral epiphysis which is not a new procedure but a refinement in technique based on preserving the periosteum on the posterior and inferior aspects of the neck of the femur, both from actual tearing and from tension. Open reduction is done without any preliminary trial of manipulation. Most poor results are caused by improper treatment, and are due to avascular necrosis in the epiphysis of the head. Necrosis in the epiphysis is caused by further damage to its blood supply through the ligamentum teres and the periosteum on the posterior and inferior aspects of the neck.

Manipulation, he believes, should be condemned except in acute traumatic cases, and it should be gentle if attempted. If reduction is not easy, closed methods should be abandoned. Patients in the so-called preslipping stage and those with minimal slipping (less than 1 cm.) are best treated by nailing in situ without reduction. When the displacement is more than 1 cm., and is gradual or has existed longer than two weeks, open reduction should be done without preliminary manipulation. In old united cases, if there is a good hip joint, intertrochanteric osteotomy may be beneficial. Later in life, arthroplasty offers much improvement for the old arthritic hips and especially for the cases with ankylosis.—*R. S. Bromer.*

Farkas, Aladár, Wilson, Milton J., and Hayner, J. Clifford. An anatomical study of the mechanics, pathology and healing of fracture of the femoral neck; preliminary report. *J. Bone & Joint Surg.*, Jan., 1948, *30-A*, 53–69.

In search of a better understanding of fracture of the femoral neck, the anatomy and mechanics of the upper portion of the femur were studied by the authors. Dissection and roentgenographic analysis of the upper portion of the shaft and neck revealed the presence of a highly independent laminar, bony system, from 10 to 12 cm. long, which begins from 2 to 4 cm. below the lesser trochanter and ends in a fanlike fashion at the cartilaginous plate of the head. This proved to be the internal weight-bearing system of the proximal portion of the femur. This system, they found, undergoes slow resorption in its distal portion after middle age, but never disappears. On the roentgenogram it can be seen throughout life from its distal to its proximal end. Microscopically, it consists of a great number of laminae and bone cells, and a rich endosteal lining. It resembles the spongy laminae of the iliac bone, hence the speed with which it is capable of new-bone formation

Mechanically, the internal weight-bearing system is a compression system, and during weight-bearing it is found to be almost in the vertical plane. The presence of tensile stresses is doubtful. Preceding adduction fractures, the internal weight-bearing system is resorbed and replaced by cortical bone in its entire distal portion. Its proximal end remains spongy, with laminar character. The separation occurs at the site where the spongy proximal portion begins and the distal cortical portion ends. In abduction fractures, the internal weight-bearing system suffers only trauma, but is otherwise healthy and strong. On this basis, the authors explain the rapid healing of such fractures.

On the basis of the anatomy and pathology of the femoral neck, two types of fracture may be distinguished: (1) compression fractures, comprising the abduction, intermedial, and adduction fractures; and (2) subcapital separations, represented by most fractures of the aged. The prognosis of the compression fractures is good, if the fragments are kept in good apposition and fixation in plaster, in Russell traction, or by nailing.—*R. S. Bromer.*

Golding, F. Campbell. Congenital coxa vara. *J. Bone & Joint Surg.*, Feb., 1948, *30-B*, 161–163.

The author suggested in a previous communication that congenital coxa vara and the short femur of micromelia were variations of the same congenital anomaly. In that paper he reported 11 patients, 1 of whom has been followed over a period of thirteen years. In this paper he adds 2 more cases.

The upper shaft of the congenitally short femur, which appears to be absent, is actually formed in cartilage though imperfectly. The roentgenographic appearances in later life depend upon the extent to which this cartilage is converted to bone. In early months, roentgenograms show only the lower portion of the shaft of the femur and there is no evidence of the upper portion of the shaft, neck or upper femoral epiphysis. When the upper femoral epiphysis appears, it leaves a broad band of cartilage in the region of the epiphyseodiaphyseal junction. The development of separate areas of ossification within this zone of cartilage gives an appearance "fragmentation" which has sometimes been mistaken for osteochondritis, and for the appearance of "triangular fragments," often described in the lower portion and sometimes in the upper part of the femoral neck. These are of no particular importance. Final ossification is delayed, weight-bearing meanwhile causing deformity or even complete solution of continuity. A second area of imperfect and delayed ossification may also be found below the trochanters where the shaft is frequenty thin, sometimes dense, and the differentiation of medulla and cortex is imperfect. The appearances are very variable because the condition develops slowly over many years.—*R. S. Bromer.*

BRONITSKY, JACOB. Chondromalacia patellae. *J. Bone & Joint Surg.*, Oct., 1947, *29*, 931–945.

The term "chondromalacia patellae" applies to a circumscribed degeneration of the articular surface of the patella, as evidenced by softening, fibrillation with eventual fissuring and erosion of the cartilage. Trauma has been suggested as an etiologic factor but in many patients no history of trauma can be elicited. Some authors have agreed that, although trauma is the primary cause, a predisposed constitution and the peculiar mechanism of the knee joint also play important roles in the formation of the degenerative changes found in the condition. The present theory is that degeneration of the patellar cartilage can exist with or without trauma. Acute trauma or static deformities can influence the origin and progress of the disease. The question of constitutional disposition and heredity as etiological factors is still unsettled.

The earliest detectable lesions are most frequently found on the medial facet, less frequently in the center and occasionally on the lateral facet of the patella. In severe cases, the entire articular surface may be involved. Roentgenograms are of almost no help in making the diagnosis in the early stages of the disease. The evidence of osteophyte formation will verify the presence of degeneration of the articular cartilage; but in a large number of cases, even osteophytes do not show in the roentgenograms. Indentation of the patellar cartilage, attributed to contusion of the articular surface has been described by Haglund. Other writers, however, have been able to show that this indentation is a frequent finding and has no relationship to trauma or to chondromalacia of the patella.

In a patient in the early years of the third decade, with a history of chronic discomfort in the knee which does not respond to conservative treatment, with also weakness of the joint, tendency to locking, occasional swelling and pain on the mesial side of the joint, the diagnosis of chondromalacia of the patella must be taken into consideration. If patellar crepitation or grating is present, this diagnosis can be made with a greater degree of certainty. In young individuals, a positive diagnosis of the condition can only be made at the time of operation.

In regard to operation the author found that patellaplasty or chondrectomy, combined with some form of covering for the articular surface, gave consistently poor results. The surgery of choice is either the partial chondrectomy or the patellectomy.—*R. S. Bromer.*

MUMFORD, E. B. Congenital dislocation of the patella. *J. Bone & Joint Surg.*, Oct., 1947, *29*, 1083–1086.

A case of congenital dislocation of the patella in a white woman, aged twenty-five, is reported. A congenital dislocation of the patella is a constant condition in contradistinction to the recurrent type of dislocation which is a changing condition. Roentgenograms of the patient showed, in the right knee, lateral displacement of the patella, the presence of a small loose body beside the lateral femoral condyle and a depression in the condyle corresponding to the size and position of the body. The roentgenographic diagnosis of dislocation of the patella was confirmed by physical examination, as well as at operation, and the case was classified as the congenital type. In the patient's family history similar trouble with the knees existed in four successive generations. Mumford recommends the operation of Conn for this condition which he believes offers a satisfactory prognosis. Congenital dislocation of the patella presents an entirely different operative problem than does the recurrent type of dislocation. As the condition progresses extensive joint changes may occur. The family history of a "knee condition" in four successive generations suggests an element of heredity on the maternal side.—*R. S. Bromer.*

HARRIS, HERBERT W., and MEYERS, SOLOMON G. Salmonella suipestifer infection of the knee joint. *J. Bone & Joint Surg.*, Jan., 1948, *30-A*, 217–219.

Salmonella suipestifer, a paratyphoid organism, also known as *Salmonella choleraesuis*, gives rise to three clinical syndromes: (*a*) acute gastroenteritis (it may be a cause of epidemics of "food poisoning"); (*b*) a typhoid-like fever due to bacteriemia, and (*c*) a pyogenic infection, in which the organism becomes localized in any one of a number of sites. Because of the absence of gastrointestinal symptoms in some infections with this organism, and because the reputation of this organism as an abscess producer is not well known, although firmly established, the authors thought it worth while to report a case of infection of the knee joint with this organism.

The patient was a negro, an army sergeant, admitted to the hospital with fever which

reached 104° F. Three days previously he had had a fracture of the femur. Pain developed in the knee joint which was aspirated and penicillin was injected into the joint. One week later because of continued high fever an arthrotomy was performed, the knee joint was irrigated and penicillin again injected. Six days later his temperature became normal and he was evacuated one month later to the Zone of the Interior in a hip spica. His later course could not be ascertained. *Salmonella choleraesuis* was isolated from the blood culture. No roentgen examination is recorded in the case report.

The patient received both sulfadiazine and penicillin in addition to local therapy to the joint so it is impossible to estimate the efficacy of the individual types of treatment. It is also impossible to estimate the role of the repeated transfusions given him or of the immunity acquired by him, in the subsidence of the disease.—*R. S. Bromer.*

Gordon, Everett J., and Shechter, Nathan. Salmonella suipestifer pyarthrosis of the knee joint. *J. Bone & Joint Surg.*, Jan., 1948, *30-A*, 220–224.

A case of infection of the knee joint with *Salmonella suipestifer* is reported. The roentgen examination of the affected knee revealed a degenerative joint lesion, osteochondritis dissecans. This had been aggravated by repeated traumas and the combination of the two may have predisposed the joint to localization of the infection. It, however, did not apparently influence the course of the infection since complete recovery occurred in three months from the time of onset, without extension of the suppurative process into adjoining bones. This might have been expected from the loss of the normal cartilaginous barrier in the region of the osteochondritic effect. The defect showed no roentgenographic change during the course of the infection.

The few cases of typhoid and *Salmonella* infections which have been treated by streptomycin have shown generally unsatisfactory results. Streptomycin was employed in this case, and clinical improvement (fall of temperature and pulse to nearly normal and decreased swelling and pain in the knee) was manifest three days after streptomycin therapy was begun. The joint cultures became negative and remained so, when sufficient streptomycin had been given.

Although the infection resolved completely and the immediate functional result was excellent, the authors believe that the degenerative changes of osteochondritis dissecans, previously present, will result in more joint disturbance at a later date.—*R. S. Bromer.*

Coleman, H. M. Recurrent osteochondral fracture of the patella. *J. Bone & Joint Surg.*, Feb., 1948, *30-B*, 153–157.

Two cases of a comparatively rare fracture of the patella are reported. The injury is undoubtedly, in the author's opinion, more frequent than would be expected, and many loose bodies removed from the knee joint have originated from such fractures. The injury is produced by the patella sliding laterally over the lateral femoral condyle and in so doing, scoring the articular surface of both patella and condyle. When the quadriceps contracts, considerable tangential force is applied, which shears off a portion of the articular cartilage of the patella, usually with a thin layer of underlying bone. In both cases reported in this paper, direct pressure had also been applied to replace the dislocated patella.

The defects in the patella could be demonstrated roentgenographically in the 2 cases reported, but lateral, oblique and "sky-line" views were necessary to secure the right projection. A pneumo-arthrogram was tried in one case but it did not make the defect any more clear. The author, however, thinks it would be of value in revealing a defect which involved only the articular cartilage of the patella. He emphasizes that osteochondral fractures of the patella should be recognized early, loose bodies removed, and defects in the articular surfaces smoothed off, or the patella removed if it is extensively involved. He recommends plication of the capsule on the medial side in order to prevent recurrence of the injury and to prevent dislocation of the quadriceps tendon in cases where the patella is removed.—*R. S. Bromer.*

Ross, Donald. Disturbance of longitudinal growth associated with prolonged disability of the lower extremity. *J. Bone & Joint Surg.*, Jan., 1948, *30-A*, 103–115.

Impaired function of an extremity during its longitudinal growth may result in a discrepancy of limb length. Paralysis, skeletal infection, trauma and congenital anomalies are among the common causes of impaired function. In such cases, the inequality of limb length is

the result of growth retardation and does not entail premature closure of the epiphyseal cartilage. However, in some patients, marked length discrepancy or alignment deformity develops and in these cases, premature closure of one or more epiphyseal discs can usually be demonstrated.

Growth retardation of the epiphyseal discs precedes permanent arrest. This retardation is due to partial degeneration of the cartilage as the result of atrophy of disuse. Arrested growth occurs later, due to complete degeneration of a portion of the epiphyseal plate and the repair of the defect so formed by a bony ridge. This complete degeneration is probably due to some secondary factor, such as the abnormal stresses present with a faulty gait.

Roentgenographic evidence of growth disturbance is usually present prior to the development of marked inequality of limb length or alignment deformity. It is usually not detected, however, because roentgenograms of the knees of these patients are not made until some factor, such as deformity, calls attention to the knee. By this time there are marked alterations in the epiphyseal cartilages, which represent advanced growth disturbance. The early changes are not observed unless repeated roentgenographic examinations are made from the onset of the disability to the end of the active growth period.

The early alterations of the epiphyseal cartilage, which are evidence of growth disturbance of the knee are thinness of the epiphyseal disc and the presence of a transverse zone of dense bone on its metaphyseal aspect. Growth retardation scars are numerous, and osteoporosis of the regional bone is pronounced. The contour of the epiphyseal cartilage is irregular with one or more peaks projecting into the metaphysis. In some instances, radiolucent defects in the metaphysis are further evidence of deranged endochondral ossification. Such changes may precede actual cessation of growth, but in some instances, recovery of normal longitudinal growth occurs.

If growth arrest does occur, roentgenograms show a bony ridge across the ephiphyseal disc. The transverse zone of bone on the metaphyseal aspect of the disc becomes wider and more dense in the region of this bony bridge, and long trabeculae converge toward its site from both the epiphysis and metaphysis.

Certain sites are more favorable for epiphyseal bridging. In the distal end of the femur, the point of arrest is commonly posterior to the central portion of the disc. The remaining disc may continue to grow, causing posterior rotation of the condyles. In the proximal end of the tibia, the arrest is often in the posterior medial quadrant, in which case continued growth of the remaining cartilage results in tibia vara. Not infrequently, the tibial tubercle unites prematurely with its metaphysis, and tibia recurvata develops. In either case proximal displacement of the fibula in relation to the tibia occurs.

Prevention of growth deformity in chronic diseases of the lower extremity is not always possible. However, Ross states, measures that shorten the duration of disability from hip disease, such as operative fusion, avoidance of prolonged immobilization, and careful supervision of the patient who resumes weight-bearing on a limb which has undergone marked osteoporosis, may minimize the chance of growth arrest. If arrest does occur, early recognition may make it possible to avoid deformity or marked discrepancy in limb length by the employment of an epiphyseal arrest operation.—*R. S. Bromer.*

Nissen, K. I. Plantar digital neuritis. *J. Bone & Joint Surg.*, Feb., 1948, *30-B*, 84–94.

Morton (1867) described with remarkable clarity the symptoms of the severe type of metatarsalagia which now bears his name: neuralgic pain felt in the sole about the fourth metatarsal joint, radiation of pain to the fourth and sometimes the third toe, onset of pain with walking and standing, and relief of pain by resting with the shoe discarded. Nissen reports a series of cases of the condition in which 27 selected patients had thirty-five operations on the sole of the foot. At operation, degeneration of the plantar digital artery to the cleft between the third and fourth toes was found to precede the fibrous thickening of the nerve described by Betts in 1940. Similar changes rarely occurred in neighboring clefts. Roentgenographic examinations showed no change except in one patient. In this case, the roentgenogram showed separation of the third and fourth metatarsals and toes. A connective tissue mass around the thickened nerve was roughly spherical and almost an inch in diameter and cast a soft tissue shadow in the web space.

Local resection of the digital nerve almost always gave complete relief from pain, and the plantar scar gave rise to no trouble. Histologic findings showed that the nerve lesion was

ischemic in nature. Nissen believes that acute pain arising as a new event in cases of "anterior flat foot" may prove to be due to this condition. He regards the condition as a distinct pathological and clinical entity which can best be described as plantar digital neuritis.—*R. S. Bromer.*

ROENTGEN AND RADIUM THERAPY

Cottentot, Paul, and Bourdon, Rene. La roentgenthérapie à bas voltage et à faible distance (radiothérapie de contact) en dermatologie. (Roentgen therapy at low voltage and short distance (contact therapy) in dermatology.) *J. de radiol. et d'électrol.*, 1946, *27*, 319–332.

This paper comprises a large series of cases treated by contact therapy in the roentgen therapy department of the dermatological center of France—Hôpital St. Louis. The report covers the treatment of 473 patients in this hospital from December, 1942, to January, 1945. Results with different types of lesions are tabulated and discussed. Epitheliomas of the skin were treated (130 cases) at 2 cm. distance (tube in contact with lesion), field not exceeding 30 by 30 mm. In 93 of the epithelioma cases a single massive dose was given with 45 kv. peak (Philips type tube), 0.2 mm. Al, and 2 cm. distance. Total dosage was 10,000 r (approximately) in 81 cases, and in 12 instances the total was from 3,000 to 6,000 r. The follow-up showed 90 per cent cured one to three years after treatment. Two epithelioma cases were treated by fractionation (1 case two seances of 5,000 r and 1 case with 5 seances of 2,000 r). Concerning radionecrosis, 3 cases developed necrosis six to twenty-six months after contact therapy and in each instance developed in cases which had been treated by divers means *before* contact therapy (electron coagulation, roentgen therapy, cauterization with acid). The remaining 343 cases included plantar and palmar warts, angiomas, keloids, nevo-carcinomas (2 successes and 2 failures), keratoses, other dermatoses, and a few lesions (11) on tongue, palate, or buccal mucosa.

The authors emphasize the fact that contact therapy in treatment of skin malignancies is very limited since it can only be used for very small lesions (not exceeding 4 cm.^{2} area and 1 cm. depth of lesion) and these are lesions which are quite easily treated by more commonly used techniques. One of the purposes of this report is to emphasize the great utility of this method in busy large hospital services where many patients must be handled rapidly and where it would be a great step if, in addition to benign lesions, certain malignant ones could be treated in from only one to several minutes.

The paper discusses the physical factors and physical problems (including the protection of the operator) involved in this type of therapy as well as the difficulty in accurately measuring the roentgens delivered to a lesion being treated with an apparatus of such high output and for such short seances; and in the conclusions formulated by the authors five major objections to this method are given fair consideration.

This is an excellent review of an extensive experience with contact roentgen therapy presented in an unbiased manner. There is a most complete bibliography appended covering this entire subject up to 1946 comprising 219 references including, of course, the American work of Pendergrass (1937 and 1939), Goin (1940), Widmann (1941), Gershon-Cohen (1941), Hodges (1941), and Quimby (1943).—*William M. Loehr.*

Watson, E. M., Herger, C. C., and Sauer, H. R. Irradiation reactions in the bladder; their occurrence and chemical course following the use of x-ray and radium in the treatment of female pelvic disease. *J. Urol.*, June, 1947, *57*, 1038–1053.

Late irradiation bladder reactions are comparatively rare and may be mistaken for carcinoma by those not familiar with the condition. The authors present a study of 164 cases of irradiation reactions in the bladders of 5,990 patients treated for uterine disease; 2,967 of these patients had cancer of the cervix, 898 cancer of the fundus, and 2,125 patients uterine fibromyoma.

Acute irradiation reactions occur during or shortly after therapy and resemble the changes occurring in the skin. In mild cases the patients have symptoms of a mild cystitis and cystoscopic examination reveals mucosal hyperemia. The more severe cases have symptoms of a more severe cystitis and cystoscopic examination reveals a diffusely red-velvet-like mucosa in which individual vessels can no longer be distinguished. In the most severe acute cases, bladder irritability may be so extreme as to result in incontinence. Cystoscopically such bladders will show partial epithelial desquamation with or without superficial erosions.

Treatment of acute irradiation reactions in the bladder consists of discontinuation of the radiation therapy, sedation, bed rest, and mild antiseptics. Recovery should occur in a few weeks, but if an excessive amount of irradiation has been delivered the reaction may become chronic. Delayed reactions with external irradiation are usually due to prior radium applications. The symptoms of late reactions are manifold. They are usually sudden in onset. Painless hematuria and dysuria are common complaints.

The chronic reactions are also divided into three groups. Grade I reactions show circumscribed areas of telangiectasis with elevated tortuous vessels. Rupture of the latter causes painless hematuria. Superficial erosions are not unusual. Grade II late reactions reveal, cystoscopically, fairly deep ulcerations, bullous edema and telangiectasis.

The greatest diagnostic and therapeutic problems are involved with the Grade III lesions. Complications overshadow the classical triad of signs: ulceration, edema, and telangiectasis. The cystoscopic picture may readily be confused with carcinoma. Histopathologically the appearance is also deceiving. Secondary infection and extensive necrosis are common Dysuria, frequency and hematuria are almost constantly present. Eventually most ulcers will heal. When healing fails to take place fistulae may develop. Eventually the upper urinary tract becomes involved from ureteral obstruction secondary to pelvic fibrosis, from ureteral occlusion due to bladder scars, or as the result of ascending infection.

Late radium reactions are due to an endarteritis, ischemia and necrosis. Histopathologically fibrosis, round cell infiltration and epithelial cell inclusions are noted. Important points in the diagnosis of late radium reactions include history of previous radium irradiation, localization of the lesion to the lower posterior bladder wall, the cystoscopic appearance, the histological appearance, and the presence of telangiectasis and fibrosis of the skin and vaginal mucosa.

Grade I lesions only require treatment if severe or persistent bleeding is present, when coagulation, cautiously applied, should be sufficient. In Grade II reactions treatment is directed toward control of secondary infection. In Grade III reactions treatment is that of existing complications. Prognosis is usually good although recovery may be delayed.

The causes of late radium reactions are excessive irradiation, individual sensitivity to irradiation, anatomical variation in the thickness of the cervix, uterus and bladder, and faulty technique in the administration of the radium. Excessive irradiation with radium appears to be the most important single cause of late radium reactions in the bladder. This may be due to an excessive dose delivered in a short time or retreatment of an area previously treated to tolerance. The authors found that dosages of less than 4,000 mg-hr. were responsible for 50 per cent of the total number of irradiation reactions and for more than 50 per cent of the Grade III reactions.

The majority of reactions occurred between the first and fourth years following radium irradiation. Forty per cent of 10 patients who received more than 6,000 mg-hr. developed reactions within one year as compared to 11.6 per cent of 112 patients who recieved less than this amount. No patient who received more than 6,000 mg-hr. developed reactions after more than four years, but 10 per cent of the 112 cases receiving less than this amount developed reactions after from five to thirteen years.

In the matter of individual sensitivity, diabetics and patients with chronic localized infections are more prone to develop reactions. Individual tolerance remains an unknown factor. The effect of variations in the thickness of the cervix, uterus and bladder on irradiation reactions is obvious. In spite of all precautions reactions will occur in some cases.

The actual incidence of late radium reactions in the bladder cannot be determined since patients with too short an interval of time since treatment may develop reactions at a later date. Many patients die of their disease before reactions can occur. Many patients with bladder lesions are never discovered.

The number of reactions has not changed appreciably with changing methods of radium application.

The prognosis of these late radium reactions is almost invariably good; 78.7 per cent of the authors' series healed. Grade I lesions had an average healing time of 4.3 months; Grade II lesions had an average healing time of 5.9 months; and Grade III lesions an average healing time of 18 months.—*Rolfe M. Harvey.*